Acute Transverse Myelitis After SARS-CoV-2 Infection: A Rare Complicated Case of Rapid Onset Paraplegia in a Male Veteran

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Case Report

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Abstract

Background: SARS-CoV-2 (COVID-19) is a new human pathogen, and currently, the world has been plagued by its pandemic and there are no specific treatment options, mostly affects the respiratory system, ranging from mild flu-like symptoms to severe acute respiratory syndrome (SARS), but extra respiratory multi-systemic involvement has also been reported.

Case presentation: A 63-yr-old Caucasian male veteran (retired army colonel), known case of controlled Type 2 diabetes, chronic renal failure and ischemic heart disease, about 4 days after the onset of flu-like syndrome (with no trauma history) experienced loss of control over both lower limbs, absent sensation from the chest below with constipation and urinary retention. Due to world SARS-CoV-2 (COVID-19) outbreak, his nasopharyngeal specimen was tested for COVID-19 reverse transcription polymerase chain reaction (RT-PCR) and positive result obtained. Chest x-ray and HRCT suggested severe pulmonary involvement. Immediately, he was admitted at emergency ward, treated based national COVID-19 protocol and a series of diagnostic procedures were started up to find out the cause of his non-heterogeneous peripheral (spinal) neuromuscular manifestations. Brain CT scan and MRI were normal, but spinal MRI with gadolinium contrast agent showing extensive increased T2 signal involves central grey matter and dorsal columns, extension between C7 and T12 with linear sagittally oriented enhancement posteriorly within the cord in the mid and lower thoracic cord. The CSF specimen obtained from LP shown pleocytosis, positive RT-PCR for SARS-CoV-2 and elevated IgG index. Clinical presentations, MRI, CSF and laboratory findings, after ruled out the other numerous possible causes with specific methods, suggested the Acute Transverse Myelitis (ATM) as a probably complication of COVID-19 infection. Intravenous methylprednisolone and then human immunoglobulin was added to treatment regimen. At the end, complete resolution of dysaesthesia, urinary retention and constipation were achieved. After continuous and long respiratory and motor rehabilitation programs, he was discharged home asymptomatic.

Conclusions: We believe that SARS-CoV-2 has a potential to produces different extra respiratory multi-systemic involvement as immune-mediated process and complexes, and this should be kept in mind whenever encounter a patient with acute onset of neurological manifestations, especially after microbial infections or vaccinations.

Background

SARS-CoV-2 (COVID-19) is a new human pathogen, and currently, there are no specific treatment options, mostly affects the respiratory system, ranging from mild flu-like symptoms to severe acute respiratory syndrome (SARS), but extra respiratory multi-systemic involvement has also been reported [1,2]. Neurological manifestations are not common but reported during the acute phase and treatment period [3]. In particular, COVID-19 is a neurotrophic, neuroinvasive, and neuroinflammatory virus. Experimental animal studies reported that they cause acute flaccid paralysis (AFP) and demyelination [4]. Although as a cause of AFP has not been reported until now [5]. Yet, there was one study reported a post-infectious

acute myelitis as probable COVID-19 complication [6].Here, we reported a very rare complicated case of early-onset ATM following a SARS-CoV-2 respiratory infection.

Case Presentation

A 63-yr-old Caucasian male veteran (retired army colonel), about 4 days after the onset of flu-like syndrome, with no trauma history, experienced loss of control over both lower limbs, absent sensation from the chest below with constipation and urinary retention. He was known case of controlled Type 2 diabetes, chronic renal failure (with no need Hemodialysis) and ischemic heart disease. His vital signs include following: oral temperature 38.6 °C, blood pressure 155/95 mm Hg, heart rate 98, respiratory rate 21 and pulse oximetry 91% on room air. He was well oriented to time, place and person with no mood or psychotic symptoms. His neurologic examination demonstrated no obvious abnormal founding in cranial nerves, cognitive function or neck rigidity. Motor system examination revealed normal bulk in all four limbs. There was hypotonia in both lower limbs. Power was grade 1/5 in both lower limbs & grade 5/5 in both upper limbs. There was no involuntary movement. All modalities of sensation were diminished below D8 level. Perianal sensations were absent but deep anal pressure & bulbo-cavernosus reflex were present. Distal tendon reflexes were absent in both lower limbs (knee & ankle) & normal in upper limbs (biceps, triceps & supinator). Superficial abdominal reflexes were present in upper quadrants & absent in lower quadrants. Plantar reflexes were bilaterally mute and cerebellar signs were absent. Bilateral pathological signs were negative.

Due to world SARS-CoV-2 (COVID-19) outbreak, his nasopharyngeal specimen was tested for COVID-19 reverse transcription polymerase chain reaction (RT-PCR) and positive result obtained. Chest x-ray and HRCT suggested severe pulmonary COVID-19 involvement (Fig. 1).

With diagnosis of complicated COVID-19 infection, he was admitted at emergency ward and treated based national COVID-19 protocol with Hydroxychloroquine (400 mg po BID 1st day then 200 mg BID for 10 days), Azithromycine (500 mg po daily for 5 days) and Ritonavir (po daily for 10 days). To find out the cause of his non-heterogeneous peripheral (spinal) neuromuscular manifestations, a series of additional diagnostic procedures were started up immediately. Brain CT scan and MRI were normal. MRI with gadolinium contrast agent was performed for excluding compressive aetiology and when no compressive cause was identified, a lumbar puncture was done to distinguish an inflammatory from a non-inflammatory condition (such as ischemia, epidural lipomatosis or fibrocartilagineous embolism). Spinal MRI with gadolinium contrast agent showing extensive increased T2 signal and expansion of the cord is seen extending between C7 and T12. The T2 signal abnormality involves central grey matter and dorsal columns. Linear sagittally oriented enhancement is seen posteriorly within the cord in the mid and lower thoracic cord (Fig. 2).

The CSF sample obtained from LP was carefully evaluated for composition (especially pleocytosis), gram staining and culture, RT-PCR for SARS-CoV-2 and IgG index. Important CSF findings and main laboratory results were summarized in table 1.

Table.1: Significant Laboratory Findings

Laboratory Tests	Results	
Arterial Blood Gas	PH = 7.28	
	Carbon Dioxide Pressure = 24.2 mmHg	
	Oxygen Pressure = 60.3 mmHg	
	Bicarbonate = 15 mEq/L	
	Oxygen Saturation = 90%	
Biochemistry	Blood Urea Nitrogen = 112 mg/dl	
	Creatinine = 5.8 mg/dl	
	Creatine Phosphokinase = 447 U/L	
	Creatine Kinase-MB = 49 U/L	
	Lactic Dehydrogenase = 821 U/L	
	Aspartate Aminotransferase = 42 U/L	
	Bilirubin Total = 1.5 mg/dl	
	Bilirubin Direct = 0.85 mg/dl	
	Albumin = 2.4 gr/dl	
	Ferritin = 1240 ng/ml	
	Iron = 5.6 umol/L	
	Interleukin 6 = 47.43 pg/ml	
	Potassium = 5.4 mEq/L	
	Sodium = 134 mEq/L	
	Magnesium = 3.8 mEq/L	
	Calcium = 7 mEq/L	
Haematology	White Blood Cell = 15000 /µL	Lymphocyte = 6%
		Neutrophil = 92%
	Red Blood Cell = 3.000.000 /µL	
	Hemoglobin = 8 gr/dl	
	Hematocrit = 25%	
	Platelet = 70.000 /µL	
	Blood Culture in 3 times = No growth	

Laboratory Tests	Results
Serology	C-Reactive Protein = ++++
	Erythrocyte Sedimentation Rate = 68
Urine Analysis	Specific Gravity = 1.002
	Protein= ++++
	Glucose= +
	Blood= ++
	White Blood Cell = 4–6 /hpf
	Red Blood Cell = 14–16 /hpf
Urine Culture	No growth
CSF Analysis	White Blood Cell (Predominately Lymphocyte) = 96 /µL (pleocytosis)
	Red Blood Cell = None
	Protein = 128 mg/dl
	Glucose = 68 mg/dl
	Gram stain = Negative
	RT-PCR for SARS-CoV-2 = Positive
	IgG index = Elevated (> 0.91)
CSF Culture	No growth

In the following, due to sudden clinical condition deterioration and acute respiratory distress syndrome (ARDS), he was transferred to intensive care unit (ICU), who underwent endotracheal intubation and ventilation support. Increased blood creatinine (5.8 mg/dl) was an indication for shaldon catheter insertion and intermittent hemodialysis. After four sessions of hemodialysis, with acceptable blood creatinine, his shaldon catheter was removed and the hemodialysis dialysis was terminated. After five days suitable intensive cares lead to significant clinical improvement and need no more ventilation support and he was extubated.

Clinical presentations, MRI, CSF and laboratory findings, after ruled out the other numerous possible causes with specific methods, suggested the Acute Transverse Myelitis (ATM) as a probably complication of COVID-19 infection (table 2).

Table.2: Numerous Possible Causes of ATM and Our Ruled out Methods

Categories	Causes		Ruled Out Methods
Parainfectious	Bacterial	mycoplasma pneumoniae, chlamydia pneumonia	Negative serum IgM
		mycobacterium tuberculosis	Negative Tuberculin skin test (Mantoux method) and T cells of tuberculosis
		Syphilis	Negative VDRL and RPR test
	Viral	Varicella Zoster (VZV), Human Immunodeficiency Viruses (HIV), Epstein-Barr (EBV), influenza B virus, adenovirus, coxsackievirus, influenza A virus, parainfluenza virus, cytomegalovirus (CMV), respiratory syncytial virus	Negative serum IgM
Systemic Inflammatory or Autoimmune Diseases	Systemic Lupus Erythematosus (SLE)		Negative serum Anti-ds-DNA, anti-Sm antibodies and anti-nucleosome antibodies
	Sjogren Syndrome		Negative serum Anti-SS-A/RO, Anti-SS-B/LA
	Antiphospholipid Syndrome		Negative serum anti-phospholipid antibody and anti-cardiolipin antibody
	Neurosarcoidosis		Normal serum CEA, ACE and calcium
	Systemic Sclerosis		Negative serum Anti-centromere antibody and anti-scl70
CNS Autoimmune Disorders	Multiple Sclerosis (MS)		Normal CSF Oligoclonal bands and serum anti-MOG antibodies
	Neuromyelitis optica (NMO)		Normal serum NMO-IgG (AQP4)

Categories	Causes	Ruled Out Methods
	Acute Disseminated Encephalomyelitis (ADEM) and Cortical Encephalitis	Normal serum anti-MOG antibodies and brain MRI
Trauma	Spinal cord compression (due to epidural abscess, tumor or haematomas)	No evidence of any space-occupying or compressive condition in spinal cord MRI

Intravenous methylprednisolone (1 gr QID for 3 days and then tapered to 1 mg/Kg/d) was added to the COVID-19 treatment regimen. Over the 3 following days his clinical condition deteriorated, with intensifying lower thoracic pain, progressing hypoaesthesia and dysaesthesia becoming more disabling and characterised by numbness and ice cold sensation. Then, methylprednisolone was replaced by intravenouse human immunoglobulin (25 gr daily for 3 days) and significant improvement was observed within the next days. One week later, the patient was able to walk unassisted, with complete resolution of dysaesthesia, urinary retention and constipation. Five weeks after admission, with continuous and long respiratory and motor rehabilitation programs, he was discharged home asymptomatic.

Discussion

Acute Transverse Myelitis (ATM), an inflammatory myelitis, is one of the causes of acute transverse myelopathy and a rare clinical condition (an estimated incidence of 3.1 cases per 100.000 patient years) with an acute inflammatory process of the spinal cord that can be classified in three distinct groups according to its etiology: myelitis due to a direct infection of the spinal cord; myelitis in the context of a systemic disease, such as leukemia or a connective tissue disorder; and myelitis with a suspected autoimmune basis. The last group is the most common form of ATM (approximately 25%-40% cases are caused by viral infections) and may occur as a post- or parainfectious condition. Respiratory and intestinal infections are important potential triggers of ATM, but some postvaccinal cases have also been reported [7–9].

The clinical picture of ATM includes acute partial or complete motor, sensory, and autonomic spinal cord dysfunction presented as paraplegia or quadriplegia, decrease or loss of deep reflexes, sensory impairment and varying degrees of bladder and bowel disturbance. Usually the full-blown disease is reached four weeks after onset, but in most cases the peak occurs in the first week with the level of involvement set at the onset [10, 11]. In a few patients, however, the disease has an ascending course with risk of asphyxia when upper cervical segments (C3-C5) are involved.

Probable hypothesis for the post or para-infectious or post-vaccinal ATM was that infectious organism was targeted against by immunologic system which also attacked central and peripheral nervous

systems because of structural similarities between the microbial cellular wall components and neuronal receptors. Viral inflammatory process result in neuronal death or spinal tract lesions or lead to increased susceptibility to opportunistic infections due to immunodeficiency. Moreover, recent study showed that SARS-CoV-2 could enter the human body through ACE2 receptors on the surface of human cells and causes disease. It was intriguing that ACE2 receptors were also expressed on the membrane of spinal cord neurons. Furtherly, suggesting that SARS-CoV-2 was implicated in acute myelitis by the specific ACE2 receptors on the surface of spinal cord neurons [6].

Differential diagnosis of an evolving myelopathy is broad (Table 2) and diagnosing viral myelitis can be challenging which made after excluding other aetiologies. Initial evaluation should focus on excluding compressive aetiology for which urgent neurosurgical evaluation is mandatory [12]. MRI with gadolinium contrast agent should therefore be obtained in a short-time period. If no compressive cause is identified, a lumbar puncture should be performed to distinguish an inflammatory from a non-inflammatory condition. If an inflammatory myelopathy is identified further evaluation should be undertaken. Clinical features, laboratory (especially CSF) studies and imaging findings provide useful information for neurological conditions [13].

Treatment of ATM is still a matter of controversy in the literature and should be tailored to the individual patient. The efficacy of antivirals, high doses intravenous methylprednisolone and immunoglobulin in viral immune-mediated neurological disorders, led some authors to use them in ATM [13]. Recent studies have confirmed its efficacy shortening motor recovery and significantly increasing the proportion of patients able to walk independently at follow-up when compared to a historical control group [14, 15].

The spectrum of clinical outcomes in viral myelitis ranges from spontaneous recovery to ascending progression and death [16]. It has been observed that functional recovery depends much on the clinical presentation. An abrupt, severe onset, rapid progression and flaccidity below the level of the lesion have the poorest prognosis [17, 18].

Conclusions

In this paper, the authors reported a very rare complicated case of early-onset ATM following a SARS-CoV-2 respiratory infection which passed several diagnostic, therapeutic and rehabilitative challenges. We only found one study reported a post-infectious acute myelitis as probable COVID-19 complication [6]. Because of the potential significant morbidity of the disease associated with poor neurologic outcome, experience gained from case reports is important. We believe that SARS-CoV-2 has a potential to produces different extra respiratory multi-systemic involvement as immune-mediated process and complexes, and this should be kept in mind whenever encounter a patient with acute onset of neurological manifestations, especially after microbial infections or vaccinations [6, 19].

Abbreviations

HRCT
High Resolution Computed Tomography
CT Scan
Computed Tomography Scan
MRI
Magnetic Resonance Imaging
CSF
Cerebrospinal Fluid
LP
Lumbar Puncture
RT-PCR
Reverse Transcription Polymerase Chain Reaction
AFP
Acute Flaccid Paralysis
ATM
Acute Transverse Myelitis
IgG
Immunoglobulin G
CEA
Carcinoembryonic Antigen
ACE
Angiotensin Converting Enzyme

Declarations

1-Ethics approval and consent to participate:

The ethical approval of this study was issued with registration N# 224 967g912 by the Ethics Committee of the Medical Faculty in Aja University of Medical Sciences.

2-Consent for publication:

I (Dr Hamze Shahali as Corresponding Author), on behalf of the authors, expresses my satisfaction with the publication of this study in that valuable journal.

3-Availability of data and materials:

All the data of this study is available and could be accessible for publication by that valuable journal.

4-Competing interests:

I declare that there is no competing interest about the authors of this study, at all.

5-Funding:

This research was our special interest to defeat the COVID-19 pandemic and so, all the expenses were paid personally. I declare that we did not use any government funds to conduct this study, at all.

6-Authors' contributions:

1-Ebrahim Hazrati, MD:

The main owner of the idea, scientific supervisor in the field of intensive care and article editor. (First Author)

2- Ramin Hamidi Farahani, MD:

The scientific supervisor in the field of Infectious diseases and article editor. (Co Author)

3- Amir Nezami Asl, MD:

The scientific supervisor in the field of military medicine, biological defense and article editor. (Co Author)

4- Hamze Shahali, MD. MPH. AME:

The data collector and researcher, main author of the article, Scientific and literary editor, Main scientific and executive supervisor. (*Corresponding Author)

7-Acknowledgements:

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Figures

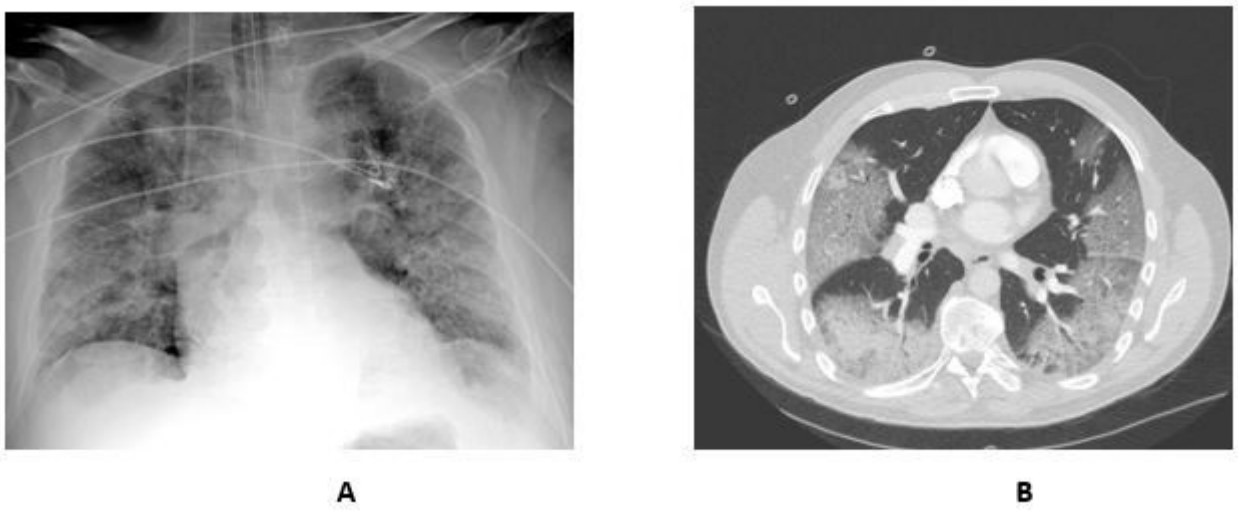

Figure 1

Severe Radiographic Pulmonary COVID-19 Involvement. A: CXR and B: Chest HRCT

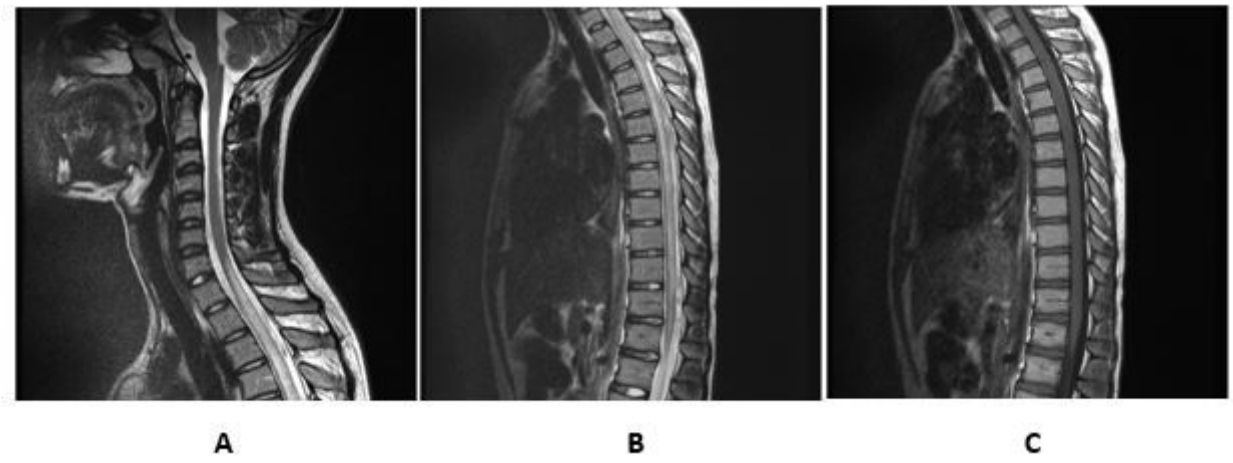

Figure 2

Spinal MRI with Gadolinium Contrast Agent, A and B: Sagittal T2 Views. C: Sagittal T1 View