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Case Report
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An Uncommon Presentation of SARS-CoV-2 Infection: A Case Report

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Abstract

Introduction: SARS-CoV-2 emerged in Wuhan city of China in December 2019 and rapidly spread to more than 200 countries. The respiratory system is the most commonly affected. Many case reports have emerged which show neurological symptoms and signs, although rare neurological symptoms should be expected and treated promptly. We hereby present a relatively rare case of COVID-19 related encephalitis.

Case Report: A 21-year-old female with no significant comorbidities, who was tested positive for COVID-19 4 weeks ago and was self-isolating, came to the hospital with H/o high fever of 38.8°C, and altered mental status. She was febrile and delirious in the Emergency Department. Repeat testing of COVID-19 was positive. MRI showed an area of subtle restricted diffusion, Lumbar puncture was done, which was indicative of viral meningitis. Viral panels for all the known viruses that cause meningitis were negative. COVID-19 PCR in CSF could not be sent because of non-availability. EEG showed abnormal slowing with no epileptiform discharges. She was given IV antibiotics, acyclovir and Keppra, after which her mentation improved in 2 days. She was discharged on day 4 after discontinuation of all antimicrobials.

Discussion: COVID-19 is majorly known to cause respiratory illness in patients with multiple comorbidities. Nervous system symptoms are uncommon but prevalent. Most of the nervous system signs are from strokes which are secondary to coagulopathies. Encephalitis-like syndromes are very less noted in COVID-19, and even when noted carry bad prognosis. This case is unique for the fact that it is present in a 21 year old with no known co-morbidities and had a quick resolution.

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Introduction

SARS-CoV-2 emerged in Wuhan city of China in December 2019 and rapidly spread to more than 200 countries [1]. World Health Organization made a report of its first case on Dec 31, 2019. By Jan 07, 2020, genetic analysis of viral isolates from affected patients indicated that the etiologic agent was a novel coronavirus distinct from those causing Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS) [2]. As of Mar 11, 2020, COVID-19 had been recognized in 172 countries and was declared a global Pandemic [3].

As of Jun 01, there were 6,264,742 cases and 375,513 deaths [JHU.edu].

The respiratory system is the most commonly affected; neurotropism also has been shown in some case reports. According to some observational studies, COVID-19 patients have presented with complaints of headache, nausea, vomiting, myalgia, dizziness, [4] hypogeusia, hyposmia, and impaired consciousness [5] symptoms that are consistent with the involvement of nervous system. The exact mechanism by which SARS-CoV-2 penetrates the Central Nervous System (CNS) is not known. However, there are two theories which might have an explanation for CNS symptoms:

1. Hematogenous spread from the systemic circulation to cerebral circulation, wherein the slower blood flow is conducive to the virus, which damages the capillary endothelium and gains access to the brain.

2. Dissemination through the cribriform plate and olfactory bulb [6].

Neurological complications in COVID-19 infected patients have not been widely reported [7]. Especially in young patients who are usually asymptomatic from the disease.

Case Presentation

A 21-year-old Caucasian female with no significant past medical history comes with a history

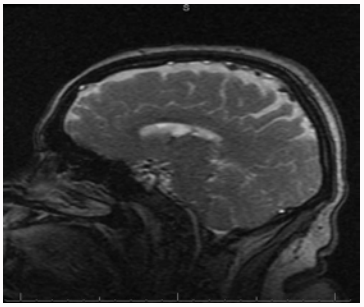

Figure 1: MRI image depicting restricted diffusion in corpus callosum.

Table 1: Lumbar puncture was done suspecting meningeal infection, given fever and altered mental status.

CSF Cell Count WIT		Component	Value
Clarity CSF	Clear…	WBC CSF	820
Micro ACC#	6000215535	Mono/Macrophage CSF	100
Micro/Monophage CSF	100	Polys CSF	0
Polys CSF	0	RBC CSF	70
RBC CSF	70	Clarity CSF	Clear
			Colorless
Supermat Color CSF	Clear…	Supermat Color CSF	Clear
WBC CSF	820		Colorless

Table 2: CSF Culture.

CSF Culture	No Growth 05 Days
Grain Stain Result	Few WBCs
	No Organism Seen

Table 3: Components values.

Component	Value	Units
IgG CSF	21.5	1.0-5.0 MG/DL
Albumin CSF	104	8.0-35.0 MG/DL
CSF IgG as Present	12.7	%
Albumin Percent	61.5	%

Table 4: Status.

Oligoclonal Bands
Negative

of altered mental status with agitation and confusion. There was no history of nausea, vomiting, headaches, seizure-like episodes, as per her mother.

She was tested COVID-19 positive following a week of cough and fever. She was doing well and self-isolating with on and off episodes of fever. After 20 days of being tested positive, she developed a fever of 101 and altered mental status. There were no focal neuro-deficits or other abnormalities. In the emergency department, her temperature was 38.4°C; she was not oriented and was delirious. Her HR, RR and Blood pressure were within normal limits. Examination was limited because of delirium, but there were no motor deficits. COVID-19 was retested, which came back to be positive. The urinary drug screen was negative.

CT brain was unremarkable.

MRI showed an area of subtle restricted diffusion, which could be consistent with a cytotoxic lesion of the corpus callosum (Figure 1).

Table 5: Different tests.

Test Name	Result	Flag	Ref-Ranges	Units	Site
Cytomegalovirus (CMG) IgG Antibody	<0.20		<0.60	U/mL	WMRL
Interpretation:					
Negative: No antibody detected					
Cytomegalovirus (CMG) IgG Antibody	<8.0		<30.0	AU/mL	WMRL

Table 6: Epstein-Barr Virus DNA, Quant Real-Time, PCR CSF.

Source	<CSF		QCRL
EBV DNA, QN PCR	<200	copies/mL	QUESC
Log EBV DNA, QN PCR	<2.30		QUESC

Table 7: Specimen Information: Cerebrospinal Fluid.

Component	Value	Ref Range and Units	Status
Eschericia Coli K1	Not detected	Not detected	Final
Haemophilus influenza	Not detected	Not detected	Final
Listeria monocytogenes	Not detected	Not detected	Final
Neisseria Meningitidis	Not detected	Not detected	Final
Streptococcus agalactiae	Not detected	Not detected	Final
Streptococus pneumoniae	Not detected	Not detected	Final
Cytomegalovirus	Not detected	Not detected	Final
Enterovirus	Not detected	Not detected	Final
Herpes Simplex Virus 1	Not detected	Not detected	Final
Herpes Simplex Virus 2	Not detected	Not detected	Final
Human Herpesvirus 6	Not detected	Not detected	Final
Human Parechovirus	Not detected	Not detected	Final
Varicella Zoster Virus	Not detected	Not detected	Final
Cryptococcus neoformans/gattii	Not detected	Not detected	Final

Table 8: Specimen Information.

Component	Value	Ref Range and Units	Status
Adenovirus	Not detected	Not detected	Final
Coronavirus 229E	Not detected	Not detected	Final
Coronavirus HKU1	Not detected	Not detected	Final
Coronavirus NL63	Not detected	Not detected	Final
Coronavirus OC43	Not detected	Not detected	Final
Human Metapneumovirus	Not detected	Not detected	Final
Human Enterovirus/Rhinovirus	Not detected	Not detected	Final
Influenza A	Not detected	Not detected	Final
Influenza B	Not detected	Not detected	Final
Parainfluenza Virus (PIV) 1	Not detected	Not detected	Final
Parainfluenza Virus (PIV) 2	Not detected	Not detected	Final
Parainfluenza Virus (PIV) 3	Not detected	Not detected	Final
Parainfluenza Virus (PIV) 4	Not detected	Not detected	Final
Respiratory Syncytial Virus	Not detected	Not detected	Final
Bordella Parapertussis	Not detected	Not detected	Final
Bordella Pertussis by PCR	Not detected	Not detected	Final

This assay identifies 4 separate strains of seasonal Coronavirus, but does not detect COVID-19.

Lumbar puncture was done suspecting meningeal infection,

Table 9: Scanned Result.

Scanned Result
NEGATIVE
Comment: Test performed by Mayo Clinical Laboratories Rochester, MN
Lab and Collection
Misc send out Lab West Nile PCR on spinal fluid - 06/1/2020

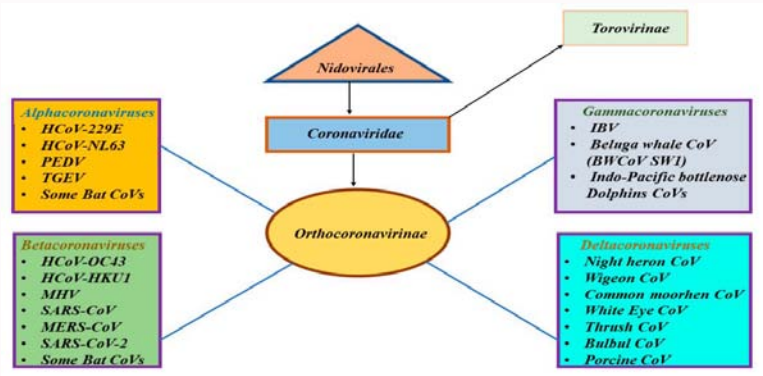

Figure 2: classification of Coronaviruses [8].

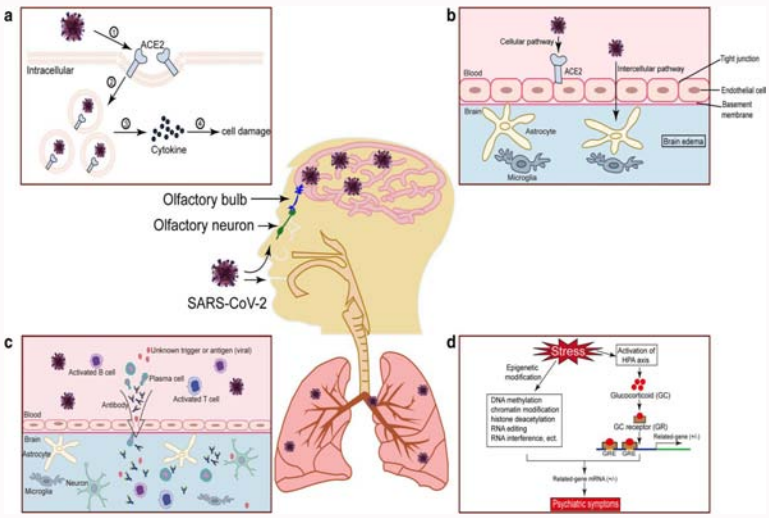

Figure 3: Mechanism of SARS-Cov-2 spread to CNS [6].

given fever and altered mental status. The results are depicted in the tables (Tables 1-9).

She was initially started on vancomycin, ceftriaxone, Acyclovir for broad coverage, as the LP was more suggestive of viral infection, and Acyclovir was continued. Meanwhile, her blood culture was negative, and all the viral PCR were negative as illustrated above.

Tests were done to rule out cytokine storm, which showed normal IL-6, D-Dimer was elevated at 8.2, ferritin and procalcitonin were normal.

EEG was done, which showed mixed slowing with no epileptiform discharges, she was started on Keppra as per neurology recommendations. Her mentation improved, in 2 days. Acyclovir was stooped since she was not spiking any more fevers, and Keppra was continued.

She was discharged home safely. In the retrospect, since all the investigations were done on the CSF but COVID-19 PCR was not obtained in the CSF and Serum was positive for COVID-19, it was concluded that she had COVID-19 encephalitis.

Discussion

COVID-19 had created a global challenge when it broke out as a pandemic on Mar 11, 2020. It is a severe acute respiratory syndrome secondary to SARS-CoV2. So far, 6,927,639 cases are confirmed globally and 400,290 deaths. [JHU]

COVID-19 has various manifestations, most common of which can be asymptomatic, ranging to Acute Respiratory Distress Syndrome and Multi-organ failure [1]. The most studied manifestations of the disease are often respiratory and coagulopathies [4]. Central Nervous system manifestations are most often in the form of stroke due to coagulopathies, but other symptoms have been rare and reported in small numbers [5].

Coronaviruses are positive sense, single-strand enveloped RNA viruses which belong to Coronaviridae subfamily. The name comes from the Latin corona, meaning crown. Viral envelope under electron microscopy appears crown-like due to small bulbar projections formed by the viral spike (S) peplomers. Coronaviruses and Toroviridae combined form the order Nidovirales [7,8].

Genetic analysis of SARS-CoV2 shows a high similarity to bat SARS-like virus, belonging to the beta coronavirus.

Recent research data on respiratory coronaviruses have demonstrated the capacity of these viruses to go beyond the respiratory system to enter the nervous system and establish persistent brain infection of animals with or without induction of neurological illness [9].

Some coronaviruses experimentally can spread from airway mechanoreceptors and chemoreceptors to the medullary cardio-respiratory centers [2]. Viruses can also access the nervous system *via* the circumventricular organs that generally lack a Blood-Brain Barrier (BBB) and *via* dorsal root ganglia and autonomic (including cardiac) ganglia, both of which have no Blood-Nerve Barrier (BNB) [2-4].

Endothelial microvascular dysfunction leads to vasoconstriction with subsequent organ ischemia, inflammation with associated tissue edema, and a pro-thrombotic state. Endothelial dysfunction is also an essential factor.

During the epidemic outbreaks of SARS in China and MERS in Saudi Arabia, neurological signs and symptoms were reported in small numbers of patients infected with the respiratory coronaviruses SARS-CoV-1 and MERS-CoV, respectively [8]. Additionally, SARS-CoV-2 may incite non-inflammatory encephalopathy, which has been previously implicated in SARS-CoV-1 infection. Neurological manifestations of SARS-CoV-1 include seizure, generalized polyneuropathy, mixed axonal neuropathy, and primary myopathy [10]. Similarly, in MERS, viral encephalopathy has been reported around the world.

Among the proposed treatments are the protease inhibitor drugs, remdesivir, the anti-IL6 monoclonal antimalarials (chloroquine and hydroxychloroquine), antibody tocilizumab, and convalescent serum or immunoglobulin have proven efficacy, yet more than 200 clinical trials are underway. No treatment has demonstrated high-level evidence of success with confusion, coma, ataxia, and focal motor deficits [11].

Treatment with IVIG and corticosteroids has been variable. IVIG may mitigate severe cytokine storming and alleviate secondary vasogenic edema. Seizures should be managed with AEDs and, given anecdotal evidence, anti-inflammatories/anti-parasitics, hydroxychloroquine, and viral protease inhibitors such lopinavir and ritonavir may be beneficial. Special attention should be paid to increasing intracranial hypertension by using dehydrating agents such as mannitol and furosemide. The median hospital-stay for those discharged alive is ten days Considered [5,7,12].

Various neurological aspects of coronaviruses have been reported from strokes due to coagulopathy to hemorrhagic encephalitis. Things to be noted are that with most COVID-19 associated encephalopathies the prognosis has been poor so far in the few reported cases. It is interesting to note that a young female without any comorbidities except obesity, could recover very fast and was able to return to her baseline in 2-3 days.

Conclusions

1. Although minority of patients with COVID-19 will have neurological manifestations, it is clear that SARS-CoV-2 affects the central nervous system.

2. Most of the encephalitis/encephalopathy associated with COVID-19 is in patients with multiple comorbidities and elderly, but it can also be seen in younger population with few comorbidities.

3. Contrast to older people with comorbidities, younger patients has a much benign course, with eventual recovery.

4. As we suspect fewer complications in younger populations, it is important to look out for specific symptoms which might be related to COVID-19.

5. Because some of the neurological sequela of this disease can be devastating, the neuroscience community must be aware of the neurological impact of COVID-19 and how to approach it.

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