A Young Female with SARS-CoV-2 Infection Presenting with Concurrent Neurological and Pulmonary Manifestations: A Case Report

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Coronavirus disease 2019 (COVID-19), besides its well-known deleterious effects on the respiratory system, is also reported to affect the central nervous system (CNS), presenting with neurological manifestations, that are commoner among older patients with associated co-morbidities and in the critically ill with COVID pneumonia. Infective, cerebrovascular, and hypoxic-toxic-metabolic etiology have been implicated. Reported outcomes have been poor with persistent neurological deficits among the majority who have survived. We report a young lady who presented with neurological manifestations alongside moderately severe COVID-19 pneumonia. Diagnosed early and managed as severe encephalopathy after excluding infective and cerebrovascular aetiology. Responded well to conservative measures and made a complete recovery. Early recognition of neurological manifestations of COVID-19 disease followed by the institution of appropriate therapies improved the outcomes.

Keywords: COVID-19, COVID-19 pneumonia, neurological symptoms/ manifestations, encephalopathy, encephalitis

Introduction

COVID-19 is well known for its respiratory effects. Published data suggests that over 35% of COVID-19 patients may initially present with neurological manifestations due to diverse aetiologies and mechanisms.[1] CNS involvement is commoner among older patients (>50 years) with associated co-morbidities, and among the critically ill with COVID-19 posing difficulties in recognition and demanding a high degree of alertness for early recognition to commence appropriate therapies to improve outcomes.[1]

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We report a patient who presented with neurological symptoms alongside moderately severe COVID-19 pneumonia managed as acute encephalopathy and made a full recovery within two weeks of hospital admission.

Case Report

An unvaccinated, 35-year-old lady with fever, cough, and loss of appetite for over two weeks was admitted to hospital on the 17th day of illness, in respiratory distress, and tested positive for Rapid Antigen Test (RAT) for COVID-19. On admission, she was conscious but drowsy, tachypnoeic with a respiratory rate (RR) of 60/ minute and oxygen saturation (SpO_2) of 84% on-air. Treated with oxygen 15L/minute via Non-Rebreathing Mask (NRBM), intravenous (iv) dexamethasone 6 mg, subcutaneous (sc) enoxaparin 40 mg and iv ceftriaxone 2g. Stabilized and transferred on NRBM (SpO_2 96%) to a COVID-ICU on the same day for further management. Other than for gestational diabetes mellitus, her past medical history was unremarkable.

On admission to the ICU, she was afebrile, drowsy, confused, GCS 14/15, pupils equal and reacting to light, and no neck stiffness or focal neurologic deficits; respiratory parameters were satisfactory on NRBM (RR of 35-40/min; SpO_2 96%); slightly tachycardic but stable otherwise; random blood sugar (RBS) 500 mg/dl with ketone bodies present in urine. Respiratory supports and rehabilitation were continued and glycaemic control achieved with (iv) soluble insulin on a sliding scale. High-resolution CT (HRCT) - Chest showed moderate interstitial pneumonia and minimal ground-glass opacities with a CT severity score of 15/25.

Since admission, the drowsiness, confusion, and agitation worsened and the NCCT Brain (non-contrast CT) showed slightly effaced ventricles with early cerebral oedema. As CSF was inconclusive of infection or inflammation, encephalopathy was suspected and empirically treated with (iv) dexamethasone 8mg 8 hourly for 48 hours and (iv) mannitol (20%) 250ml for 3 days. Acyclovir 500mg (iv) 8 hourly and vancomycin 1g (iv) 12 hourly were commenced to provide antiviral and antibacterial cover, respectively. MRI brain and EEG were not considered in the absence of localizing neurological features and convulsions respectively.

On Day 2 in ICU, respiratory parameters deteriorated due to sepsis however, improved with non-invasive supports (CPAP). PE was excluded by a CT-pulmonary angiogram (CTPA). Respiratory supports were stepped down gradually. Following complete recovery from CNS manifestations by Day 12 of ICU stay, discharged to the COVID ward on nasal oxygen 2L/ minute and sent home within a week.

Image 1: *CT Pulmonary Angiogram (CTPA)*

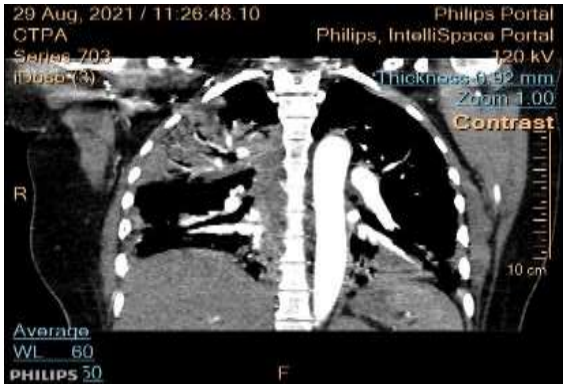

Image 2: *High-Resolution CT – Chest (HRCT) showing moderately severe COVID-19 pneumonia (CT severity A score of 15/25) and segmental consolidation*

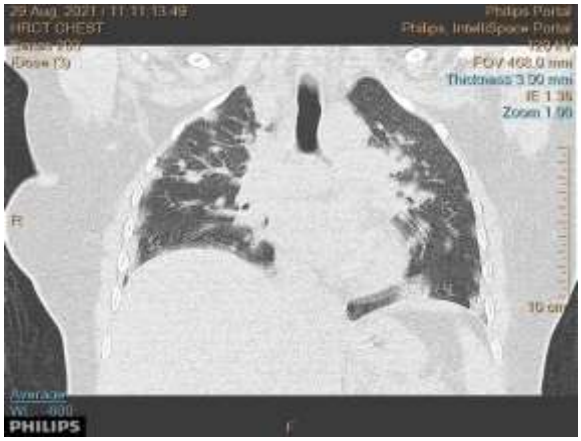

Image 3: *Non-contrast CT Brain (NCCT) showing slightly effaced ventricles with early cerebral oedema*

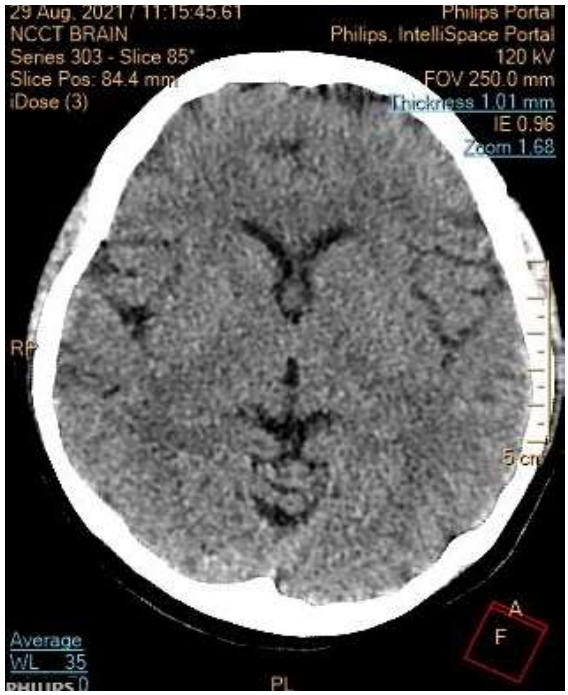

Table 1: *Clinical details and Lab reports*

Day of illness (ICU)	**D17**	**D18**	**D19**	**D20** ↔	**D24** ↔	**D28**	**D29**	**D30**
Resp Supports SpO_2%	NRBM 95-96%	NRBM 95-96	NRBM 93-94	CPAP/ NRBM 94-96	CPAP/ NRBM 94-96	VM 35% 97	VM 35% 97	NP >96
CVS	stable	stable	stable	stable	stable	stable	stable	stable
CNS GCS	Drowsy 15/15	Drowsy 15/15	Confused 12/15	Confused 12/15	Drowsy 14/15	Less drowsy 14/15	15/15	15/15
WBC per µL	8.1	8.6	10.6	13.7	20.7	17.1	16.7	11.6
Neutrophils %	85	90	92	92	90	89	86	85
Hb g/dL	11.3	12.2	12.5	13	13.3	12.4	11.8	10.3
Platelets per µL	315	358	349	354	336	334	302	310
PT/ INR		1.33	1.32	1.14	1.14	1.29	0.97	1.04
APTT		29.5	20.5	18.8	25	28		25.8
CRP mg/dL	52.3		332	216	200	102	62	35
S. Bilirubin (T)	0.26	0.51	0.56	0.68		0.66	0.88	0.71
AST/ ALT/ ALP	47/ 29/ 83	44/ 22/ 68	40/ 27	44/ 22/ 68		44/ 25	29/ 29	35/ 35/ 52
S. Proteins/ Albumin g/L	67.2/ 21.3	68/ 25.1	66.2/ 28.9	63/ 25	64.3/ 26.7		62.1/ 23.9	63/ 25
S. Creatinine mg/dL	0.81	0.91		0.68	0.71	0.81		0.54
Blood urea mg/dL	31.5	34.2	36		40	27.8		
S. Electrolytes	Normal							
RBS mg/dL	500	363	200	140	Normal			
Urine KB	positive	positive	negative					
LDH IU/L		534	539	684	720	807	399	292
S. Ferritin ng/mL			500					
D-Dimers ng/mL				723	525		391	408
PCT ng/mL		15.1		0.99	0.77	0.82	0.26	0.17
Troponin – I ng/mL			0.445	0.995				0.044
ABG								
PH	7.29	7.42	7.4	7.52	7.44	7.55		7.44
PCO_2	23	25	20	37	39	32		39
PO_2	129	152	76	56	68	82		210
Lactate	1	1.2	0.9	2.4	1.1	1.2		0.8
HCO_3^-	11.1	16.2	16.9	30	26.5	22.7		26.5
Base Deficit/ Excess	(-)15	(-) 6.8	(-) 11.9	7.3	2.3	1.3		2.3
S_aO_2	99	99	95	92	94	97		100

Case Discussion

Neurological manifestations occur in over one-third of hospitalized COVID-19 patients, and may present during the disease or as the initial or only presentation.[2,3] The aetiological mechanisms of neurologic manifestations are multi-factorial; infective, toxic-metabolic (encephalopathy), cerebrovascular (thromboembolic or heamorrhagic stroke secondary to high blood pressure caused by dysfunction of ACE2 receptors), or immune dysfunction (inflammatory or cytokines-mediated).[4,5,6] In a systematic review (n=407), reported incidences of neurological symptoms were headache (16.8%), dizziness (13.9%), altered consciousness (11.2%), and epilepsy (1.7%). Related aetiological factors were viral meningitis/encephalitis (25;6.1%), hypoxic encephalopathy (23;5.6%), acute cerebrovascular disease (6;1.4%), and encephalomyelitis (1;0.2%).[7] Neurological manifestations were commonly reported in patients with severe COVID-19 disease who are elderly with co-morbidities.[7]

However, our patient was a relatively young healthy lady who presented at the outset with moderately severe COVID-19 pneumonia along with severe and progressive CNS manifestations. Having ruled out the infective and cerebrovascular pathology, encephalopathy was considered the most likely cause of her CNS manifestations favoured by cerebral oedema on the NCCT.

Encephalopathy is characterized by diffuse brain dysfunction that typically manifests with altered consciousness, a hallmark feature ranging from confusion, and delirium progressing to deep coma, typically with no evidence of brain inflammation on CT/ MRI or on CSF analysis.[8] In a cohort study (n=2088), 55% had delirium[9] and in another study among hospitalized patients (n=509), 31.8% had encephalopathy.[8]

The aetiology of encephalopathy can be multiple with direct neuronal injury caused by hypoxaemia, toxic-metabolic abnormalities, and inflammatory-immune-mediated mechanisms.[8,9] Hypoxaemia (P_aO_2 52 to 80 mmHg; S_aO_2 92-96%) and inflammatory mediators (indicated by raised markers of inflammation - CRP, LDH, ferritin) were likely causative factors in this lady. Other than the metabolic acidosis (base deficit -15) and ketonuria present at the time of admission but normalized within 24 hours, no other metabolic causes were evident as the renal and liver functions were satisfactory throughout. Presumably, over time the respiratory supports and other therapies would have helped reverse the causal factors and facilitated recovery from the encephalopathy.

Although the role of glucocorticoids or other immunomodulatory therapies in treating encephalopathy is uncertain, a case series have shown improvement of severe encephalopathy in a minority following the use of glucocorticoids with or without plasma exchange.[10] Despite the conflicting evidence, (iv) dexamethasone was administered for 48 hours. Though encephalopathy was identified as a risk factor for poor outcomes, including longer lengths of hospital stays and functional/ cognitive impairments at discharge (5-80%), our patient made a full recovery within 3 weeks.

Conclusion

In a pandemic state of COVID-19, alertness on CNS manifestations of SARS-CoV-2 infection is beneficial for early diagnosis, and to commence specific and supportive therapies to facilitate recovery from the neurological manifestations.

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