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Case Report

COVID-19 encephalopathy, presenting with Broca's aphasia mimicking stroke

Ankit Bhardwaj[1]*, Atma Ram Sharma[2]

[1]Department of Pharmacology, ABVIMS and Dr. RML Hospital, New Delhi, India
[2]Department of Radiology, UCMS and GTB Hospital, New Delhi, India

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***Correspondence:**
Dr. Ankit Bhardwaj,
Email: drankitbhardwaj25@gmail.com

ABSTRACT

Neurological manifestations are emerging as relatively frequent complications of coronavirus disease 2019 (COVID-19), including stroke and encephalopathy. Here we reporting a case of a young male presented with acute aphasia at the emergency department. The patient has a positive history of upper respiratory tract symptoms, subjective fever, and myalgias, a week before for which he was tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) based on reverse transcription polymerase chain reaction (PCR) on a nasopharyngeal swab. An electroencephalogram (EEG) demonstrated interictal epileptiform abnormalities over the left posterior frontal lobe. Magnetic resonance imaging (MRI) axial T2- weighted image shows focal area of altered intensity appearing hyperintense involving the left frontotemporal lobes pre-dominantly the pre-central gyrus. A subtle restriction on diffusion-weighted imaging (DWI), with a minimal drop on apparent diffusion coefficient images. In contrast, it shows gyriform enhancement with suspicious adjacent meningeal thickening and enhancement. Cerebrospinal fluid was negative for antibody. Intravenous immunoglobulin (IVIG) 400 mg/kg was given for 5 days. The patient responded well to the therapy without any major clinical side effects and revealed complete resolution after 2 months.

Keywords: COVID-19, Encephalopathy, Broca's aphasia, Stroke

INTRODUCTION

Novel coronavirus disease 2019 (COVID-19) has a broad spectrum of clinical presentations and syndromes. Although COVID-19 is primarily associated with severe metabolic syndromes, electrolyte abnormalities, acute respiratory distress syndrome (ARDS), acute tubular necrosis, thromboembolic syndrome, cardiac events, including arrhythmias and myocarditis and neurologic syndromes.[1,2] Various incidence of ischemic stroke of the large artery has been reported in many young patients without any primary cardiac-risk factors. Systemic inflammatory response induced by infection plays an important role in endothelial dysfunction and coagulopathy.[3] COVID-19 associated first case of viral encephalitis was reported by Beijing Ditan in March 2020. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was confirmed by genome sequencing in cerebrospinal fluid (CSF) of inpatients.[5] Since then, there have been increasing reports of the development of encephalitis in moderate to severally ill COVID-19 patients.[6-8] These patients have fair morbidity and mortality rate.

Steroids and immunosuppressive drugs have a wide range of anti-inflammatory effects including inhibition of the synthesis of pro-inflammatory cytokines, induction of apoptosis of T-lymphocytes and reduction of leucocyte trafficking.[9] They are the last resort and life saviour drugs used to prevent and treat the hyperinflammatory phase of COVID-19 as there are no defined standard treatment guidelines for post-infectious encephalitis.

We are reporting the case of a young adult investigated for acute Broca's aphasia mimicking infract, evolving to encephalopathy.

CASE REPORT

A 28-year-old man without any comorbidities presented with a complaint of a single episode of new-onset seizure, confusion and focal neurological symptoms including Broca's aphasia difficulty in swallowing in neuro-emergency. The patient has a history of falls in the bathroom and loss of consciousness. The patient woke up on the bathroom floor and noted a tongue bite. There was no incontinence or impaired awareness associated with it. The seizure was unwitnessed. The patient has a positive history of upper respiratory tract symptoms, subjective fever, and myalgias, a week before for which he was tested positive for SARS-CoV-2. The patient was home isolated and was on symptomatic treatment. As per the attendant, the patient experienced facial twitching and there were episodes of intermittent confusion for 2 days before the fall and the onset of a seizure.

On physical examination, heart rate (HR) 84 beats per minute, respiratory rate (RR) was 17 times per minute, temperature 98.4°F, oxygen saturation 98% on room air, and blood pressure (BP) 110/74 mmHg. The patient was well oriented on neurological examination, with intact memory and cognition. The patient had a normal gait with no motor or sensory nerve weakness (5/5).

The complete blood cell count (CBC), comprehensive metabolic panel and c-reactive protein were within the normal limits. Blood and urine cultures were also negative. Electroencephalography (EEG) demonstrated interictal epileptiform abnormalities over the left posterior frontal lobe. MRI axial T2- weighted image shows focal area of altered intensity appearing hyperintense involving the left frontotemporal lobes pre-dominantly the pre-central gyrus. A subtle restriction on diffusion-weighted imaging (DWI), with a minimal drop on apparent diffusion coefficient (ADC) images. In contrast, it shows gyriform enhancement with suspicious adjacent meningeal thickening and enhancement (Figure 1).

Cerebrospinal fluid (CSF) was sent for routine, microscopy and antibody screening. CSF studies showed lymphocytic pleocytosis, (WBC 110/mm^3; normal <5 µl of CSF), a glucose level of 86 mg/dl, a protein level of 57 mg/dl. CSF cultures for bacterial and viral cultures were negative. Antibody screening was negative for N-methyl-D-aspartate receptor (NMDA-R), glutamic acid decarboxylase (GAD), leucine-rich, glioma inactivated 1 (LGI1) antibodies, contactin-associated protein-like 2 (CASPR2), ganglioside antibodies and a panel of anti-neuronal antibodies in serum and CSF. Antibodies against the Anti-dipeptidyl-peptidase-like protein 6 (DPPX) and Anti-glycine receptor antibodies were negative (Table 1). Intravenous immunoglobulin (IVIG) 400 mg/kg was given for 5 days. The patient responded well to the therapy without any major clinical side effects. Patient discharged on tablet deflazacort 30 mg tapered slowly, over the weeks. Due to clinical improvement, CSF analysis was not repeated but follow-up cranial MRI after 2 months was done, revealing complete resolution (Figure 2).

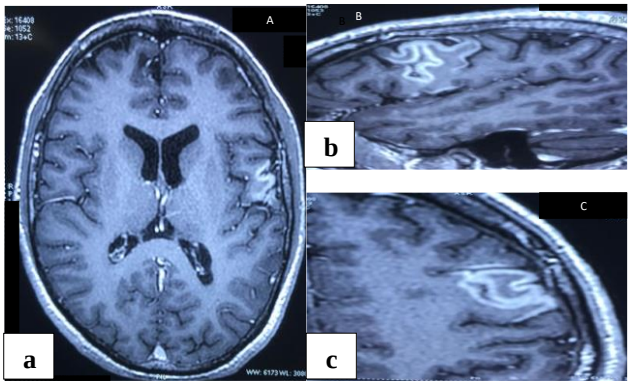

Figure 1: (a) MRI axial T2- weighted image shows focal area of altered intensity appearing hyperintense involving the left frontotemporal lobes pre-dominantly the pre-central gyrus; a subtle restriction on DWI, with a minimal drop on ADC images; (b) and (c) in contrast, shows gyriform enhancement with suspicious adjacent meningeal thickening and enhancement.

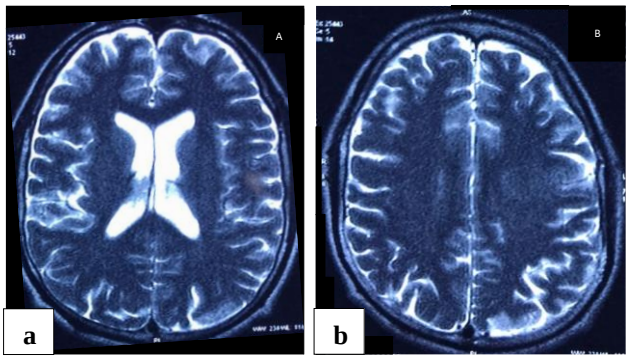

Figure 2: (a) and (b) MRI axial T2- weighted image shows complete resolution of the hyperintense focal area of altered intensity in the left frontotemporal lobes.

Table 1: Patient pertinent laboratory values.

Pertinent Laboratories	Laboratory value	Reference range
Lupus anticoagulants	0.3	≥1.2 is considered positive
Antiphospholipid antibodies	0.0	>12 IgM
		>12 IgG considered positive
Anti-NMO (neuromyelitis optica)	Negative	Not detectable in healthy subjects

Continued.

Pertinent Laboratories	Laboratory value	Reference range
Aquaporin 4 (IFA)	Negative	Not detectable in healthy subjects
Cardiolipin Ab (IgG)	7	0-14 GPL -negative
		15-19 GPL -indeterminate
		20-80 GPL -low to moderately positive
		81 GPL or above -High positive
Cardiolipin Ab (IgM)	6	0-12 MPL -negative
		13-19 MPL -indeterminate
		20-80 MPL - low to moderately positive
		81 MPL or above -high positive
PT (seconds)	10	10-12
aPTT (seconds)	26	30-45
INR (ratio)	0.8	1:2
D-dimer (ng/ml)	12	0- 230
Erythrocyte sedimentation rate (ESR) (mm/hour)	16	0 and 15
C-reactive protein (mg/l)	7	<10
Lactose dehydrogenase (LDH) (units/l)	132	100-190
Homocysteine (µmol/l)	20	normal <15

DISCUSSION

COVID-19 affects multiple-system of the body but primarily targets the respiratory system. Involvement of the nervous system is common. Neurological manifestations are reported as the result of direct invasion of the virus and seen as encephalitis, cerebrovascular accident (CAD), or rhabdomyolysis.[5-7,10,11] Immune-mediated effects are late and have been reported as Guillain-Barré syndrome, transverse myelitis, and Miller Fisher syndrome.[12-14]

Our patient in this case report presented with acute Broca's aphasia presents as an acute stroke. The patient had a history of upper respiratory tract symptoms, subjective fever, and myalgias, a week before for which he was tested positive by RT-PCR for SARS-CoV-2. The positive serum serology and WBCs pleocytosis in CSF suggested post-infectious encephalitis. The COVID-19 virus-related systemic inflammation may lead to coagulopathy and vascular endothelial dysfunction, which have already been reported earlier in young age patients without any positive cardiovascular-related risk factors, familial hypercholesteremia and anticoagulation disorder.[15] A focal status epilepticus (aphasic status) was also excluded from diagnosis based on the absence of any abnormalities in electroencephalography (EEG).[16] Atypical neoplastic changes are excluded from differential diagnosis because of the quick changes in MRI changes in response to steroid therapy.

COVID-19 induced encephalopathy have shown to have different manifestations, varying in range, and severity, which can be characterized by subacute or acute onset and progression or fluctuations course and reversibility.[17] Speech disturbance has already been reported as an early feature, but only a handful of cases mimicking and presenting as an acute stroke has been reported so far.[18] Immediate and dramatic clinical responses have been observed to corticosteroids and various immunomodulatory treatments, intravenous immunoglobulins, and plasmapheresis, suggesting immune-mediated pathogenesis of COVID-19-related encephalopathy/encephalitis.[19,20]

Post-microbial infectious encephalitis is an immune-mediated disease that typically occurs within two to four weeks. The most common presentation is acute disseminated encephalomyelitis presented as symptoms related to widespread involvement of subcortical white matter.[21] Encephalopathy, seizure, focal neurological deficits, and headache are common clinical presentations.[22] In this case, the focal area was left-frontotemporal lobes (Broca's area) resulting in aphasia. The CSF examination typically shows a lymphocytic or mixed pleocytosis, which was also seen in this patient. There are no defined standard treatment guidelines for post-infectious encephalitis. Clinical management options include a high dose of steroids or intravenous immunoglobulins.

CONCLUSION

The present case expands the literature describing post-COVID-19 infection-related immune-mediated neurological sequelae affecting the central nervous system (CNS). While confirmed causative factors are difficult to prove, the temporal profile of clinical symptoms and evidence of inflammation on MRI after 1 week following COVID-19 infection implicates SARS CoV-2 as a contributing factor.

However, it cannot be ruled out whether the clinical improvement in this patient could have been a part of the natural history of his illness. Nevertheless, the present case highlights a positive possible role of steroids in suspected patients with post-COVID-19 autoimmune encephalitis, after excluding appropriate clinical mimics.

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