Received: 17 October 2023 | Revised: 13 December 2023 | Accepted: 14 December 2023

DOI: 10.1002/ccr3.8357

CASE REPORT

Clinical Case Reports Open Access WILEY

Dementia and epilepsy following COVID-19 infection in a 25-year-old female: A case report

Farea Ahmed[1] | **Muskan Asim Taimuri**[1] | **Areeba Ikram**[1] | **Anusha Sumbal**[1] | **Sajjad Ali**[2] | **Mahfuza Anan**[3]

[1]Department of Medicine, Dow University of Health Sciences, Karachi, Pakistan

[2]Department of Medicine, Ziauddin Medical University, Karachi, Pakistan

[3]Department of Medicine, Bangladesh Medical College, Dhaka, Bangladesh

Correspondence
Mahfuza Anan, Department of Medicine, Bangladesh Medical College, Dhaka 1209, Bangladesh.
Email: mahfuzaanan980@gmail.com

Key Clinical Message

Significant atypical neurologic signs have also been recorded in COVID-19 individuals, along with a variety of other extra-pulmonary indications. The COVID-19 virus is neuro-invasive and holds significant potential to produce some unconventional neurologic manifestations

KEYWORDS

cognitive impairment, COVID-19, dementia, epilepsy, SARS-Cov-2 virus

1 | INTRODUCTION

Soon after the novel SARS-CoV-2 virus emerged in the Wuhan district of China during December 2019, it became a global pandemic.[1] The clinical manifestation of COVID-19 varies from mild respiratory discomfort to multi-organ involvement and, in the worst cases, death.[2] Along with other extra-pulmonary manifestations, significant neurologic events in COVID-19-infected patients have been reported.[1,2] Patients complained of insomnia, headache, agitation, and a degree of cognitive impairment.[1] In addition, there was an increasing trend in the incidence of stroke, seizure, coma, encephalopathy, and other neuropathic events.[1]

Neurologic diseases are a class of disorders in which cerebral dysfunction produces many sensory, motor, or cognitive impairment.[3] One of the common neuropathic illnesses includes dementia, traditionally known as forgetfulness.[4] Dementia is a neuropsychiatric syndrome affecting one's ability to resume daily life due to severe underlying cognitive impairment.[5] Reportedly, 90% of patients suffer behavioral and intellectual changes, including aggression, rage, irritation, depression, and psychosis.[5] Moreover, delusion and hallucination due to dementia-related psychosis account to be the leading causes of inpatient admission.[5] The peak incidence of this neurologic illness occurs in the two extremities of ages.[4,6] It is known to be classically observed in infants less than 1 year or senile patients over 60.[6] As mentioned, the COVID-19 virus is neuro-invasive and holds significant potential to produce some unconventional neurologic manifestations.[1]

Following current clinical case reporting guidelines, we report an unprecedented case of dementia and new-onset epilepsy following COVID-19 infection in a 25-year-old female.[7]

2 | CASE PRESENTATION

A 25-year-old female known case of new-onset epilepsy secondary to COVID-19 infection presented through the Out-Patient Department (OPD) of a tertiary care

hospital in Karachi with features of increased forgetfulness, including short- and long-term memory loss since the past 10 months. Ten months prior to her presentation to the OPD, the patient exhibited high-grade fever (103°F), nausea, anosmia, malaise, and one episode of seizure which prompted her to seek medical attention from a general physician at a local hospital. A PCR test for COVID-19 yielded a positive result. She was advised for symptomatic treatment by Tab. paracetamol 500 mg thrice a day, and non-pharmacological interventions such as taking steam and hot liquids. The severity of COVID-19 infection was moderate. During the acute phase of the illness, the patient also experienced generalized tonic–clonic seizures (GTCS) lasting for a period of 3 h, for which she was treated in the emergency department for status epilepticus and was prescribed Tab. Levetiracetam 500 mg twice daily. Based on these events, a clinical diagnosis of COVID-19-induced Central Nervous System (CNS) infection was made; however, due to a limitation of resources at the local hospital, a lumbar puncture could not be performed that could have assisted in confirming the findings further. Two weeks after the onset of initial symptoms, a follow-up COVID-19 PCR test yielded a negative result. Despite the resolution of the acute phase of COVID-19, the patient continued experiencing GTCS, necessitating the continuation of Tab. Levetiracetam 500 mg twice daily. It should be noted that the patient had non-progressive mild cognitive impairment of unknown origin since childhood which presented as forgetful tendencies such as misplacing things, as well as intellectual disabilities. Four weeks after the initial diagnosis of COVID-19, however, there was a progressive decline in her memory function. The patient was unable to recall names of her immediate family members, which she was able to do before. Her capacity to perform activities of daily living, such as cooking, cleaning, dressing, etc., became severely compromised. Agitated behavior and disorientation to place and person was also evident. However, she was oriented to time. Slowness of movement caused frequent falls and difficulty in walking.

There was, however, no history of focal neurological deficits, headache, diplopia, dysarthria, or vertigo. Notably, on further inquiry, the patient's mother mentioned the patient exhibiting delayed crying at birth. However, there was no APGAR score or other previous diagnostic test carried out to confirm the extent and severity of perinatal asphyxia (PA). There was no former diagnosis made for hypoxic brain injury (HBI) or cerebral palsy (CP). There was no previous evidence of an mini-mental state examination (MMSE) score. For this reason, her mild cognitive impairment was unknown in origin, which further worsened after the COVID-19 infection.

TABLE 1 Mini-mental state examination score.

Categories	Score
Orientation	4/10
Registration	3/3
Attention and calculation	1/5
Recall	1/3
Language	2/9
Total	11/30

On examination, her higher mental functions were not intact, with a MMSE score of 11 out of 30 (Table 1).[8] Her speech was normal but with low volume. No signs of meningeal irritation with pupils bilaterally equally reactive to light (BERL) were present. Her gait was broad-based and spastic. Her motor exam revealed normal bulk and tone in all four limbs with 5/5 powers in all muscle groups with normal (+2) reflexes in both upper limbs and exaggerated knee and ankle reflexes (+3) in both lower limbs with bilaterally upgoing plantars (Table 2). Her sensory exam, cranial nerves, and cerebellar function could not be assessed due to lack of patient's mental capacity to comprehend the examination(s).

Baseline and specific investigations were carried out to rule out CNS infection and reach an accurate diagnosis. A complete blood count and iron profile revealed that the patient was mildly anemic secondary to iron-deficiency anemia (IDA) (Table 3). Other baseline investigations were within normal limits. Furthermore, a urine detailed report was positive for trace protein and pus cells but no presence of bacteria possibly contributing to adverse effects caused by the patient's current medication, that is, Tab. levetiracetam.

Magnetic resonance imaging (MRI) of brain and orbit plain and with contrast was carried out, with findings suggesting mild cerebral atrophy with the widening of sulci in both the cerebral hemispheres and mild dilatation of the supratentorial ventricular system (Figure 1). In addition, a slightly reduced caliber of the corpus callosum, optic chiasm, and optic nerves was also noted (Figure 2). However, no evidence of demyelinating disease, hemorrhage, infarct, or space-occupying lesion was notably present.

A lumbar puncture was planned for further investigations and analysis, but the patient refused to consent. Based on the clinical findings and investigations, the patient was managed as a case of early-onset dementia and new-onset epilepsy secondary to COVID-19 infection. She continued to be given Tab Levetiracetam 500 mg twice daily to control her seizures. And Tab. Iberet folate 500 mg once a day for IDA. Furthermore, the patient's family was counseled for early-onset dementia the adverse and the adverse effects of anticonvulsants. The patient was discharged to

TABLE 2 Motor examination score.

	Left upper limb	Right upper limb	Left lower limb	Right lower limb
Tone	Normal	Normal	Normal	Normal
Bulk	Normal	Normal	Normal	Normal
Power	5/5	5/5	5/5	5/5
Reflexes	+2 (bicep)	+2 (bicep)	+3 (knee)	+3 (knee)
	+2 (tricep)	+2 (tricep)	+3 (ankle)	+3 (ankle)
	+2 (brachioradialis)	+2 (brachioradialis)		
Plantar	N/A	N/A	Upgoing	Upgoing

TABLE 3 Baseline investigations of the patient on admission.

Parameters	Current result	Unit	Normal reference range
Complete blood count			
Hemoglobin	10.0	g/dL	Male: 13.0–17.0 Female: 11.5–15.4
Hematocrit	30.1	Vol%	Male: 40–50 Female: 35–47
RBC	3.86	$\times 10^1$/L	Male: 4.5–5.5 Female: 3.8–5.2
MCV	74	fL	76–100
MCH	25.4	pg	27–32
MCHC	32.8	g/dL	31–34
WBC	5.5	$\times 10^9$/L	4.0–11.0
Neurophils	74	%	40–80
Lymphocytes	23	%	20–40
Eosinophils	01	%	01–06
Monocytes	02	%	02–10
Basophils	00	%	<01
Platelet count	230	$\times 10^9$/L	150–450
Iron profile			
Serum ferritin	8.75	ng/mL	20–250
Serum iron	30	µg/dL	70–180
Serum TIBC	411	µg/dL	260–410

follow-up after 1 month in the OPD. Unfortunately, the patient lost to follow-up.

3 | DISCUSSION

We have described the case of a young female patient with MCI before the COVID-19 infection that progressed to early-onset dementia post-infection. A thorough literature search was conducted on the PubMed database for all studies with full text available in English and original data on patients with cognitive impairment and dementia following a recent COVID-19 infection published between June 2020 and April 2023. The following keywords are cognitive impairment, cognitive dysfunction, cognitive decline, dementia, COVID-19, and SARS-CoV2. We found a total of 3 published articles with 3 cases of cognitive impairment following a recent COVID-19 infection (Table 4).

The neurological damage resulting from the SARS-Cov-2 virus is already a well-established fact. According to Ling et al., more than one-third (36.4%) of hospitalized COVID-19 patients in Wuhan, China, presented with neurologic manifestations.[12] In a study by Helms et al., 33% of hospitalized COVID-19 patients presented with a dysexecutive syndrome consisting of disorientation, poorly organized movements, and inattention.[13] Coronavirus holds a high affinity for nervous cells, thereby producing such

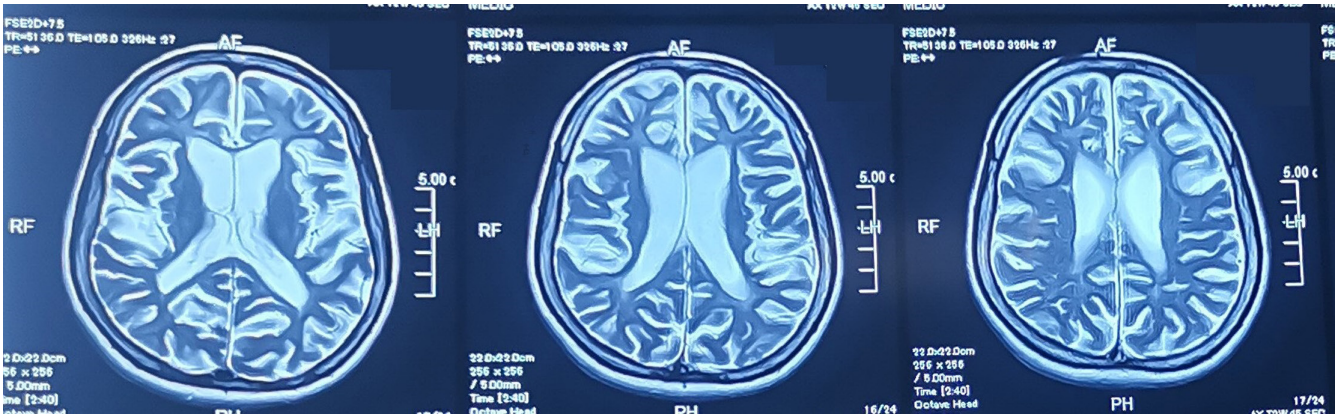

FIGURE 1 MRI of the brain with contrast showing mild cerebral atrophy with the widening of sulci in both the cerebral hemispheres and mild dilatation of the supratentorial ventricular system.

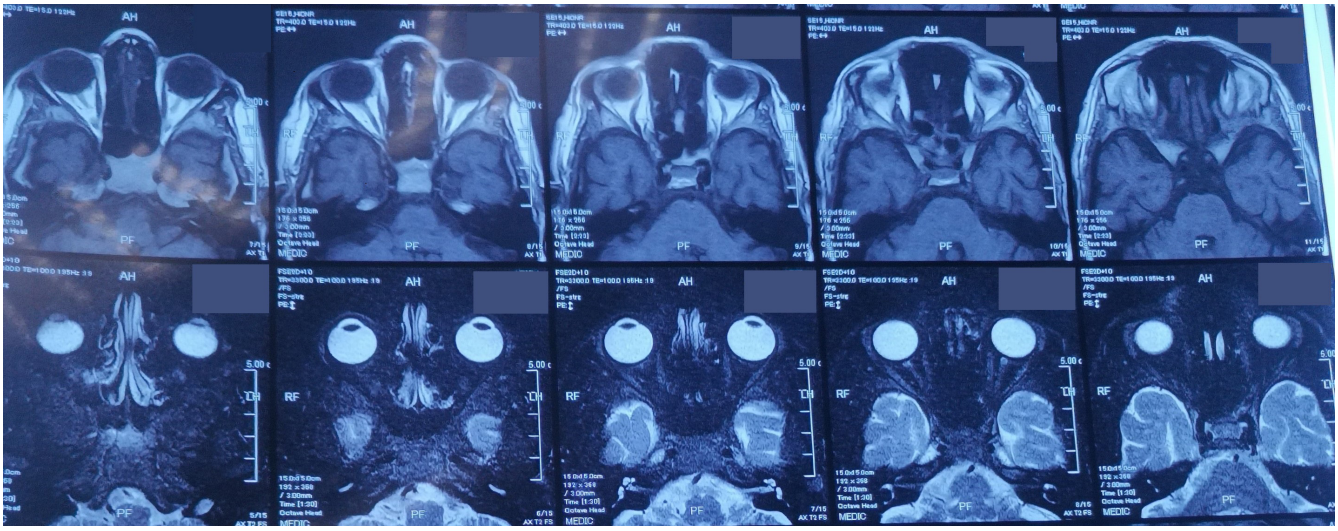

FIGURE 2 MRI of the brain and orbit with and without contrast showing slightly reduced caliber of the corpus callosum, optic chiasm, and optic nerves.

findings. Multiple routes exist for SARS-CoV-2 invasion of the CNS, including hematogenous and neural pathways. The hematogenous course is characterized by viral invasion of the endothelial cells lining the blood–brain barrier (BBB) or the blood-cerebrospinal fluid barrier (BSFB).[14] The upregulation of pro-inflammatory cytokines and chemokines can cause severe disruption of the BBB, allowing the virus to invade the CNS via the hematogenous route.[15]

The neural route takes the form of viral invasion of the olfactory nerves by binding to the angiotensin-converting Enzyme 2 (ACE2) receptor enzymes on the olfactory epithelium.[16] The entorhinal cortex (EC) is an essential element of the hippocampal formation located in the medial temporal lobe in primates. It serves as a mediator of information entering and leaving the hippocampus. It is known that damage to the EC can lead to sensory integration deficits and spatial learning impairment.[17] Therefore, the axonal transport of SARS-CoV-2 through the olfactory bulb could damage the entorhinal cortex and hippocampus, resulting in cognitive decline. Findings of anosmia in our patient during the acute phase of COVID-19 infection can contribute to the positive findings of early-onset dementia later on, as evidenced by the literature.[18]

The patient is a suspected case of PA, considering the undocumented history of delayed crying at birth that would have resulted in the failure of the neonate to begin breathing successfully. Studies have shown that infants and children who experienced PA can exhibit memory impairment which is associated with bilateral hippocampal volume reductions or abnormalities in the putamen, ventral thalamus, and putamen. This pattern of brain injury manifests as impairments in episodic and working memory and low academic attainments.[19] An acute episode of PA results in low Apgar scores and is often followed by a diagnosis of neonatal

TABLE 4 A Literature review of the case reports regarding cognitive impairment following a recent COVID-19 infection.

Age, gender	Onset of cognitive dysfunction	Clinical features	Treatment	Outcome
51 years, Female[9]	2 months after COVID-19 symptoms	Subacute/progressive severe deterioration of neurological function including cognition, speech, language, and motor skills and psychosis	Azithromycin (4-day course) to prevent bacterial infection. Cefdinir (300 mg twice daily) for suspected bacterial infection. Aspirin (81 mg daily) to prevent inflammation and coagulopathy. Ondansetron (as needed) for nausea. Aripiprazole (15 mg daily) and diazepam (5 mg twice daily) for psychosis. Cholecystectomy. Sertraline (50 mg daily) for depressive disorder. Hydroxychloroquine (200 mg daily) and osteopathic manipulative treatment for rheumatoid arthritis	Communication improved but she continued to demonstrate problems with her memory, executive functioning, and ability to formulate plans
59 years, Female[10]	Acute stage of COVID-19	Impairments in executive control, working memory, attention and concentration, processing speed, emotional regulation, and mood	Daily intake of vitamins B, C, and D. 10-day course of antibiotics. 7-day course of dexamethasone. Melatonin and aspirin at night	Subsequent to the negative PCR test outcome, the patient continued experiencing the symptoms with fluctuating intensity and frequency for a period of approximately 3 months postmorbidly
44 years, Female[11]	7 days after COVID-19 symptoms	Confusion, disorientation, apraxia and memory and thought disorder	Cefpodoxime, acetaminophen, and levocetirizine, for 5 days. IV ceftriaxone (4 g/d), vancomycin (2 g/d), acyclovir (1.5 g/d), levetiracetam (1 g/d), saline 0.9% (1.5 L/d), and mannitol (300 mL/d). High-dose intravenous methylprednisolone (1 g/d for 5 days) for acute hemorrhagic necrotizing encephalitis	The patient died

encephalopathy (NE). The signs of NE appear within the first 7 days after birth and are typically described in three stages in order of increasing severity: Stage 1 is characterized by hyperalertness or hyperexcitability, Stage 2 by lethargy, hypotonia, and suppressed primitive reflexes, and Stage 3 by flaccidity, stupor, and absent primitive reflexes.[19] In our case, it is difficult to establish whether the mild cognitive impairment was a result of delayed crying because there is no record of the Apgar score at birth and no signs of NE that could have hinted towards brain injury significant enough to cause cognitive impairment.

Although the patient did experience MCI of unknown origin since childhood, her cognitive functioning drastically deteriorated after the diagnosis of a COVID-19 infection. Sudden inability to perform activities of daily living, falls during walking, increased forgetfulness, and delirium point towards a drastic and abrupt decline in cognitive and motor performance. A low MMSE score of 11 out of 30 and cerebral atrophy on MRI assisted in diagnosing neurodegenerative dementia.[8,20,21] Our patient's deep tendon reflexes were evaluated through a motor exam that revealed hyperreflexia in both lower extremities and a positive Babinski sign. These findings indicated corticospinal tract dysfunction (CSTD).[22] The patient also developed de novo status epilepticus (SE), for which she was treated with an anticonvulsant. Although seizures are not a widely reported symptom of COVID-19, clinical or subclinical acute symptomatic seizures can be expected in patients due to hypoxia, multi-organ failure, metabolic derangements, and cerebral damage.[23]

A review of the literature helped us identify several studies reporting an increasing trend in age-related neurologic damage in the patient population affected by COVID-19. These cohorts primarily represented the senile population and those at the severe end of the disease spectrum. Interestingly, however, a UK-wide surveillance study about the neurological and neuropsychiatric complications of COVID-19 documented a disproportionate number of neuropsychiatric manifestations in the young population, with the altered mental status being identified across all age groups.[24] These findings align with our case, refuting any age-related neurologic symptoms in COVID patients. This is the first case report of our region that reports early-onset dementia and epilepsy as a neurological manifestation secondary to COVID-19 in a patient as young as 25 years of age.

Understanding the burden on healthcare infrastructure created during the COVID-19 pandemic and the importance of adequate information in disease management, we believe that the findings yielded by the case could be potentially helpful in the prospective understanding and treatment of similar presenting cases in the future. Several signs and symptoms have been reported in COVID-19 patients that indicate neurologic dysfunction. Because these findings significantly impact the prognosis and treatment of the disease, further attention is pertinent to optimize treatment and improve COVID-19 neuroscience health policy.

Our case report presents significant limitations. First, a lumbar puncture could not be performed due to the absence of patient consent. This procedure would have been vital in confirming the diagnosis of a COVID-19-induced CNS infection. Throughout the acute COVID-19 infection and even after testing negative, there was a noticeable decline in both cognitive and motor performance. These symptoms were ongoing through the initial course of COVID-19 infection, and even 10 months after that, the patient's condition progressively worsened, which prompted her to visit the tertiary care set-up. Although our hypothesis is speculative, the existing literature does indicate potential neurocognitive implications of COVID-19. Another major limitation pertains to the patient's lack of attendance for follow-up sessions despite counseling which could have provided valuable insights into the progress of her cognitive performance and epilepsy status. Thus, considering the limitations of this study, more prospective studies with well-supported data are needed to validate or reject the findings.

4 | CONCLUSION

We hereby conclude the case of progressive early-onset dementia and epilepsy secondary to a PCR-confirmed COVID-19 infection. Although pathophysiological mechanisms are still unclear, the reported CNS involvement manifesting in disorientation, forgetfulness, and motor deficits in this young patient potentiates a causal association of these factors with COVID-19 infection. Substantiating an inherent link between the two has been a topic of extensive research lately. However, this is the first case reporting these associations in a young patient. Thus, considering the limitations of this study, more prospective studies with well-supported data are needed to validate or reject the findings associated with this, which could further amplify the prognosis.

AUTHOR CONTRIBUTIONS

Farea Ahmed: Conceptualization; data curation; investigation; resources; supervision; writing – original draft. **Muskan Asim Taimuri:** Data curation; formal analysis; methodology; resources; software; writing – original draft; writing – review and editing. **Areeba Ikram:** Data curation; formal analysis; investigation; methodology; writing

– original draft. **Anusha Sumbal:** Formal analysis; investigation; methodology; writing – original draft. **Sajjad Ali:** Supervision; validation; writing – original draft; writing – review and editing. **Mahfuza Anan:** Supervision; writing – review and editing.

FUNDING INFORMATION
None.

CONFLICT OF INTEREST STATEMENT
None of the authors have any conflict of interest.

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT
Our institution does not require ethical approval for reporting individual cases or case series.

CONSENT
Written Informed Consent was obtained from the legally authorized representative of the subject with possible cognitive impairment for the publication of the case report.

ORCID
Muskan Asim Taimuri https://orcid.org/0000-0001-9457-6411
Sajjad Ali https://orcid.org/0000-0002-8024-5942

REFERENCES
1. Sharifian-Dorche M, Huot P, Osherov M, et al. Neurological complications of coronavirus infection; a comparative review and lessons learned during the COVID-19 pandemic. *J Neurol Sci*. 2020;417:117085.
2. Abboud H, Abboud FZ, Kharbouch H, Arkha Y, El Abbadi N, El Ouahabi A. COVID-19 and SARS-Cov-2 infection: pathophysiology and clinical effects on the nervous system. *World Neurosurg*. 2020;140:49-53.
3. Thijs RD, Surges R, O'Brien TJ, Sander JW. Epilepsy in adults. *Lancet*. 2019;393(10172):689-701.
4. Gale SA, Acar D, Daffner KR. Dementia. *Am J Med*. 2018;131(10):1161-1169.
5. Aarsland D. Epidemiology and pathophysiology of dementia-related psychosis. *J Clin Psychiatry*. 2020;81(5). doi:10.4088/JCP.AD19038BR1C
6. Khoujah D, Cobb MJ. Neurologic emergencies at the extremes of age. *Emerg Med Clin North Am*. 2021;39(1):47-65.
7. Gagnier JJ, Kienle G, Altman DG, Moher D, Sox H, Riley D. The CARE guidelines: consensus-based clinical case reporting guideline development. *BMJ Case Rep*. 2013;2013:bcr2013201554.
8. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*. 1975;12(3):189-198. doi:10.1016/0022-3956(75)90026-6
9. Reeves RR, Willoughby SG. Significant cognitive impairment likely associated with COVID-19 infection with relatively nonsevere symptoms. *J Osteopath Med*. 2022;122(3):119-123. doi:10.1515/jom-2021-0195
10. Damianova M. Neuropsychological and psychological dysfunctions associated with coronavirus disease 2019: a case report. *J Med Case Reports*. 2021;15:523. doi:10.1186/s13256-021-03104-w
11. Ghosh R, Dubey S, Finsterer J, Chatterjee S, Ray BK. SARS-CoV-2-associated acute hemorrhagic, necrotizing encephalitis (AHNE) presenting with cognitive impairment in a 44-year-old woman without comorbidities: a case report. *Am J Case Rep*. 2020;21:e925641. doi:10.12659/AJCR.925641
12. Mao L, Jin H, Wang M, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. *JAMA Neurol*. 2020;77(6):683-690.
13. Helms J, Kremer S, Merdji H, et al. Neurologic features in severe SARS-CoV-2 infection. *N Engl J Med*. 2020;382(23):2268-2270.
14. Li Z, Liu T, Yang N, et al. Neurological manifestations of patients with COVID-19: potential routes of SARS-CoV-2 neuroinvasion from the periphery to the brain. *Front Med*. 2020;14(5):533-541.
15. McCray PB Jr, Pewe L, Wohlford-Lenane C, et al. Lethal infection of K18-hACE2 mice infected with severe acute respiratory syndrome coronavirus. *J Virol*. 2007;81(2):813-821.
16. Meinhardt J, Radke J, Dittmayer C, et al. Olfactory transmucosal SARS-CoV-2 invasion as a port of central nervous system entry in individuals with COVID-19. *Nat Neurosci*. 2021;24(2):168-175.
17. Davis AE, Gimenez AM, Therrien B. Effects of entorhinal cortex lesions on sensory integration and spatial learning. *Nurs Res*. 2001;50(2):77-85.
18. Kay LM. COVID-19 and olfactory dysfunction: a looming wave of dementia? *J Neurophysiol*. 2022;128:436-444. doi:10.1152/jn.00255.2022
19. De Haan M, Wyatt JS, Roth S, Vargha-Khadem F, Gadian D, Mishkin M. Brain and cognitive-behavioural development after asphyxia at term birth. *Dev Sci*. 2006;9(4):350-358. doi:10.1111/j.1467-7687.2006.00499.x
20. Molloy DW, Standish TI. A guide to the standardized mini-mental state examination. *Int Psychogeriatr*. 1997;9(Suppl 1):87-150.
21. Pantano P, Caramia F, Pierallini A. The role of MRI in dementia. *Ital J Neurol Sci*. 1999;20(5 Suppl):S250-S253.
22. van Gijn J. The Babinski reflex. *Postgrad Med J*. 1995;71(841):645-648.
23. Asadi-Pooya AA. Seizures associated with coronavirus infections. *Seizure*. 2020;79:49-52.
24. Varatharaj A, Thomas N, et al. Neurological and neuropsychiatric complications of COVID-19 in 153 patients: a UK-wide surveillance study. *Lancet Psychiatry*. 2020;7(10):875-882.

How to cite this article: Ahmed F, Taimuri MA, Ikram A, Sumbal A, Ali S, Anan M. Dementia and epilepsy following COVID-19 infection in a 25-year-old female: A case report. *Clin Case Rep*. 2024;12:e8357. doi:10.1002/ccr3.8357