

A dramatic course of COVID-19-associated meningoencephalitis without respiratory involvement: a case report

Djebbi O., Imene N., Ben abdellaziz M., Lotfi L., Bhourri I., Ons K, Bounatirou C., Ben lassoued M., Lamine K.

Emergency Department, Military Hospital of Tunis, Tunisia.

Abstract

Even though COVID-19 affects mainly the respiratory system, neurological complications have been widely reported. We report a case of a 27-year-old female who was brought to the emergency department with severe confusion and abnormal behavior. The cerebrospinal fluid polymerase chain reaction (PCR) for SARS-CoV-2 was positive. Brain MRI findings were consistent with meningoencephalitis. The treatment was started accordingly, but the evolution was unfortunate, and the patient died two weeks later. Therefore, neurological symptoms should be always kept in mind by physicians during the COVID-19 pandemic. Early diagnosis may prevent death.

Keywords: COVID-19, Meningoencephalitis, Neurological symptoms, SARS-COV2.

INTRODUCTION

On March 11th, 2020, the novel coronavirus disease 2019 (COVID-19) was announced as a global pandemic. It is caused by the SARS-CoV-2 virus (severe acute respiratory syndrome coronavirus 2). While the first data suggested a purely respiratory infection, reports are emerging of neurological manifestations due to SARS-CoV-2, which range from milder presentations such as headache, dizziness, olfactory or taste dysfunction to severe complications such as seizures, stroke, Guillain-Barre syndrome, and meningoencephalitis. Although rare, these neurological manifestations are sometimes the sole initial presenting complaint of COVID-19. It is important to increase awareness of these rare

presentations among physicians and healthcare workers and facilitate early diagnosis and management to prevent the horizontal spread of the disease.

Case report

This report is about the case of a 27-year-old female patient who did not suffer from any comorbidities and did not have any history of substance abuse or alcohol intake. She has also never been to a foreign country. She was confirmed positive for SARS-COV2 infection with mild symptoms in December 2020 for which she was self-isolated and received an out-patient symptomatic treatment with good response.

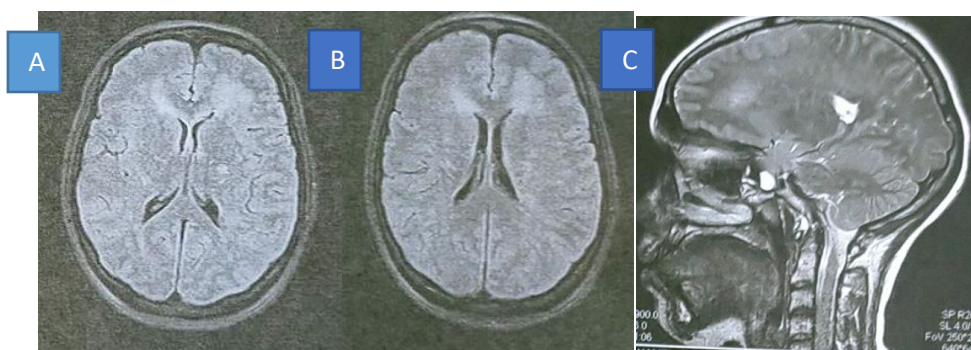


Figure 1. Fluid-attenuated inversion recovery (FLAIR) axial images (A, B) and sagittal T2 images (C) show asymmetric bilateral hyperintensity in frontal and temporal regions, mostly involving the white matter.

On late Mars 2021 (Day 1) the patient complained of headaches, generalized fatigue, vomiting, and fever of over 40 degrees Celsius (104 degrees Fahrenheit). She was treated with antipyretic agents and vitamins by her general practitioner but did not undergo any COVID-19 testing. The symptoms resolved under treatment. One week before her admission to the ED (Day 9), she became prostrate, and apathetic and developed muscular twitching. On April 2021 (day 14), the patient became disoriented, and she was brought to the ED by her parents.

Upon admission (Day 14), her vital signs were stable: RR=16cpm, oxygen saturation=100%, HR=85bpm, BP=130/70mmHg); clear bilateral lung sounds; normal cardiovascular examination; no obvious EKG abnormalities; normal blood sugar level and no fever. Neurological examination revealed acute confusion (GCS=13/15), neck stiffness, rigid limbs with exaggerated deep tendon reflexes, diffuse hyperesthesia, no focal neurological deficits, and normal cranial nerves.

Laboratory results were remarkable for a normal white blood cell count of 7400/ mm³, lymphocytes of 1550/ mm³, platelets of 221000/ mm³, and hemoglobin of 13.4 g/dl. The serum electrolytes panel, muscular enzymes (CPK, LDH), and CRP levels were within normal limits.

A brain computed tomography scan showed no acute abnormality.

A Brain MRI was performed. Diffusion-weighted images (DWI) showed hyperintensity in the frontal and temporal lobes bilaterally (Figure 1).

Shared decision-making was conducted with the patient's family and a lumbar puncture (LP) was performed due to concern for meningoencephalitis showing a clear and colorless cerebrospinal fluid and a normal opening pressure of 20 cm H₂O (normal range 10–20 cm H₂O).

The patient was started empirically on IV acyclovir, vancomycin, and ceftriaxone. She also received Sodium valproate and Clobazam for seizure prophylaxis.

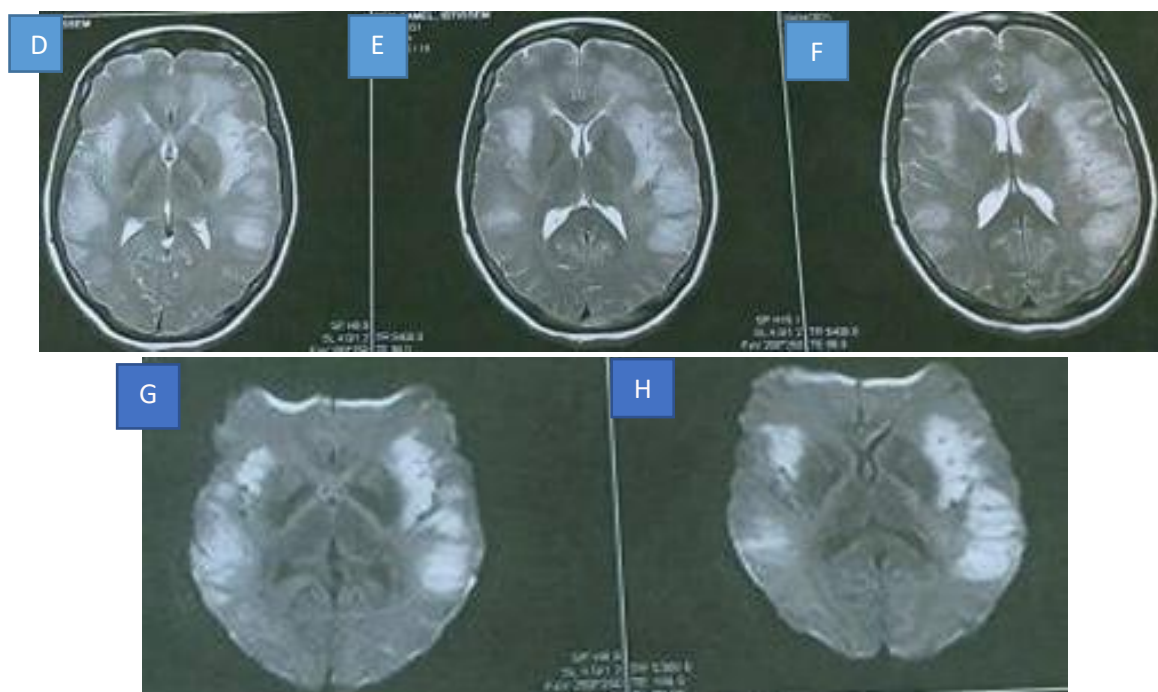


Figure 2. Axial fluid-attenuated inversion recovery FLAIR images (D, E, F) show hyperintensity in bilateral frontal-parietal-temporal and insular regions involving grey and white matter. Diffusion-weighted images (G, H) show hyperintensity with restricted diffusion.

The cerebrospinal fluid (CSF) laboratory analysis showed: a leukocyte count of 30 cells/mm³ (90% lymphocytes), 20 red cells/mm³, protein level of 2.4 g/L (normal value: 0.16 – 0.40 g/L), and glucose of 2.4 mmol/L (CSF glucose/blood glucose = 0.4). Gram's stain showed no bacteria.

A polymerase chain reaction (PCR) multiplex in CSF for several neurotropic viruses including cytomegalovirus, enterovirus, herpes simplex virus 1 and 2, human herpesvirus 6, and varicella-zoster virus showed negative results.

The determination of SARS-CoV-2 by reverse transcriptase polymerase chain reaction (RT-PCR) was performed using a nasopharyngeal swab and CSF because we assumed that SARS-CoV-2 was involved in the outbreak. Although the specific SARS-CoV-2 RNA was not

detected in the nasopharyngeal swab, it was detected in CSF.

The chest x-ray as well as a chest CT were normal.

Treatment was carried out with IV human immunoglobulin (0.4g/kg daily for 5 days), and Methylprednisolone (1g daily for 3 days) with Enoxaparin (40 mg once a day) that was prescribed for deep venous thrombosis prophylaxis.

During the second day of ED hospitalization (Day 15), the patient presented with generalized convulsive status epileptics. She was intubated and started on Levetiracetam (1g two times per day), in addition to IV Sodium Valproate (1600mg per day). The patient was subsequently transferred to the intensive care unit where a second brain MRI was performed, one week

after her admission (Day 21), revealing extended lesions (Figure 2) and venous thrombosis (Figure 3).

The evolution was unfortunate 13 days after her admission to the ED (day 27), the patient presented bilateral mydriasis and passed away 3 days later.



Figure 3. Axial T2 weighted image (I) showing hypo intensity of the left anterior vein of pellucid septum related to thrombosis

DISCUSSION

The literature review reveals that while the most common presenting symptoms of COVID-19 are fever fatigue and mild respiratory symptoms like dry cough and shortness of breath, there is a dramatic range of symptoms related to this disease such as headaches, anosmia, dysgeusia, meningitis, encephalitis, and acute cerebrovascular accidents (1)

This case indicates that neurological symptoms can be the sole manifestation of COVID-19, and highlights the neurotropic potential of SARS-CoV-2.

To date, the underlying pathophysiological mechanisms through which SARS-CoV-2 reaches the central nervous system (CNS) are

not fully understood, however, the direct neuroinvasion and, mainly, the neurological sequelae due to the systemic innate-mediated hyper-inflammation are involved (2).

CONCLUSION

Neurological symptoms can be the first presentation of covid-19. This information should be kept in mind especially during the pandemic period to prevent delayed diagnosis or misdiagnosis and to avoid the adverse outcome of the disease.

REFERENCES

1. Esposito G, Pesce M, Seguella L, Sanseverino W, Lu J, Sarnelli G. Can the enteric nervous system be an alternative entrance door in SARS-CoV2 neuroinvasion? *Brain Behav Immun.* 2020 Jul;87:93–4.
2. Iaconetta G, De Luca P, Scarpa A, Cassandro C, Cassandro E. Meningoencephalitis Associated with SARS-Coronavirus-2. *Transl Med UniSa.* 2020 Dec 31;23:42–7.
3. Netland J, Meyerholz DK, Moore S, Cassell M, Perlman S. Severe acute respiratory syndrome coronavirus infection causes neuronal death in the absence of encephalitis in mice transgenic for human ACE2. *J Virol.* 2008 Aug;82(15):7264–75.
4. Mao L, Jin H, Wang M, Hu Y, Chen S, He Q and al. Neurologic Manifestations of Hospitalized Patients With Coronavirus Disease 2019 in Wuhan, China. *JAMA Neurol.* 2020 Jun 1;77(6):683–90.
5. Poyiadji N, Shahin G, Noujaim D, Stone M, Patel S, Griffith B. COVID-19-associated Acute

Hemorrhagic Necrotizing Encephalopathy: Imaging Features. *Radiology*. 2020 Aug;296(2):E119–20.

6. Wu Y, Xu X, Chen Z, Duan J, Hashimoto K, Yang L and al. Nervous system involvement after infection with COVID-19 and other coronaviruses. *Brain Behav Immun*. 2020 Jul;87:18–22.

7. Lv P, Peng F, Zhang Y, Zhang L, Li N, Sun L and al. COVID-19-associated meningoencephalitis: A case report and literature review. *Exp Ther Med*. 2021 Apr;21(4):362.

8. Román GC, Spencer PS, Reis J, Buguet A, Faris MEA, Katrak SM and al. The Neurology of COVID-19 revisited: A proposal from the Environmental Neurology Specialty Group of the World Federation of Neurology to implement international neurological registries. *J Neurol Sci*. 2020 Jul 15;414:116884.