

## Demyelinating Lesions Following SARS-COV2 Infection: Highlighting the Problems through 2 Cases

Hajar Andour<sup>1\*</sup>, R Saouab<sup>1</sup>, I En-Nafaa<sup>1</sup>, Jamal El Fenni<sup>1</sup>, Mohamed Lahkim<sup>1</sup>

<sup>1</sup>Department of Radiology, Mohammed V - Military Hospital, Rabat, Morocco

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\***Corresponding author:** Hajar Andour. Department of Radiology, Mohammed V - Military Hospital, Rabat, Morocco

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### ABSTRACT

Since its declaration as a pandemic disease on March 2020, a multitude of cases related to the infection by the COVID-19 were documented around the world. Initially infecting the respiratory system, SARS-COV-2 engendered different lesions of the whole organs with different explaining theories. Central nervous system (CNS) was one of the main affected systems of which the frequency of manifestations led to the apparition of the term neuro-COVID19. Lesions are of great variability including hemorrhagic, ischemic and inflammatory ones with different suggested mechanisms. We report 2 cases of 2 women who developed a clinical symptomatology of stroke 3 and 8 weeks following a documented respiratory infection with COVID-19. We discuss through these cases, the possible mechanisms, the enigmas still surrounding this infectious disease as we emphasize the importance of imaging in setting the diagnosis.

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**Keywords:** SARS-COV2; Neurologic involvement; Demyelinating-MRI

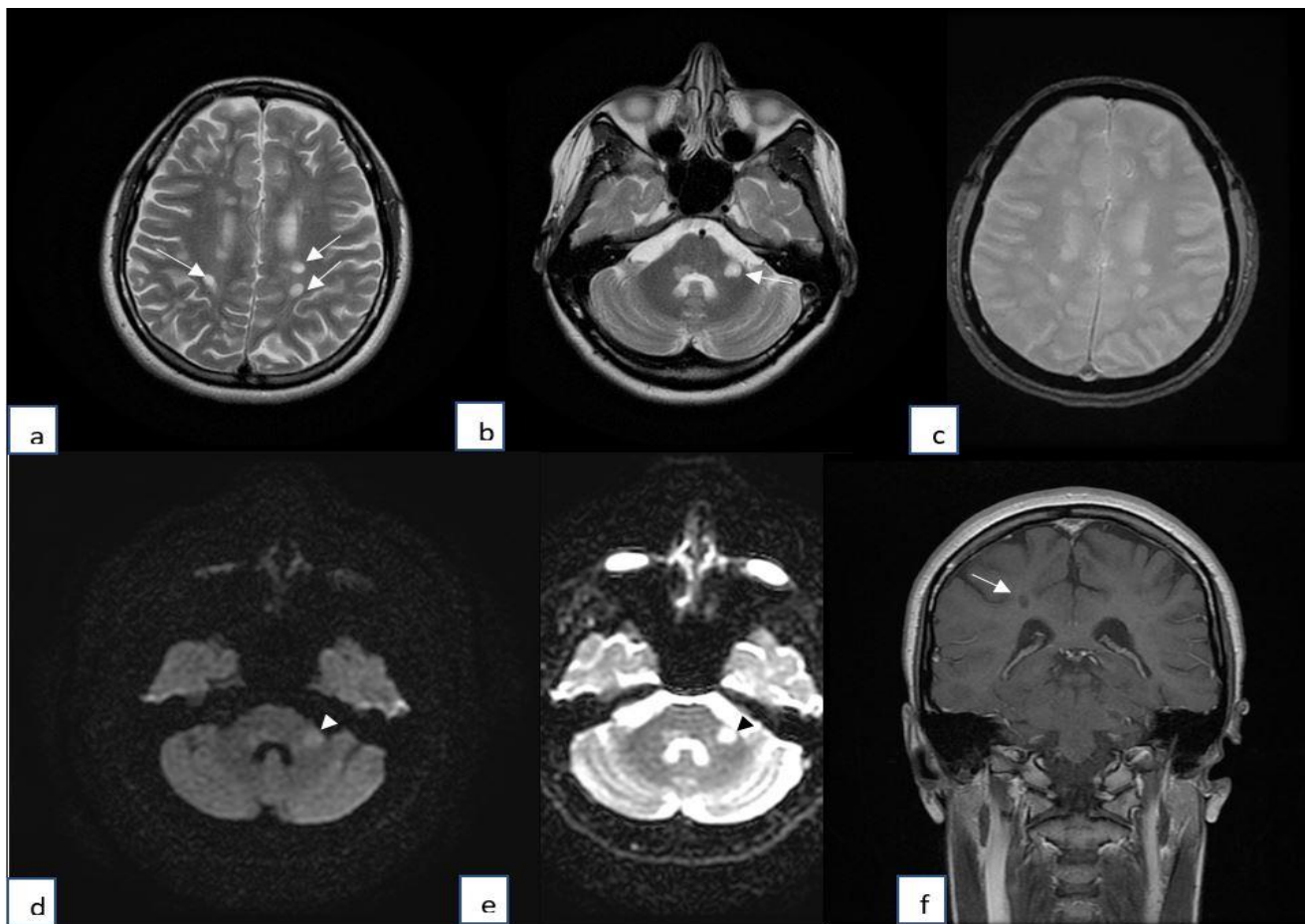
## INTRODUCTION

COVID-19 is a highly contagious disease resulting from infection with a positive-strand RNA virus belonging to the large group of corona viruses called SARS-COV2. The respiratory system remains the main target of the virus, the symptoms of which have been closely studied. However, the multivisceral disease has evolved with the appearance of several neurological and neuropsychiatric manifestations revealing the neurotropic and neuroinvasive properties of this virus which have received less attention. Several theories have been proposed but no exact pathological mechanism has been confirmed. The rapid mutation of the virus genome is hampering scientific research and resulting in more virulent variants of concern emphasizing the need to be aware of these pathological aspects and to develop diagnostic and therapeutic strategies to deal with them.

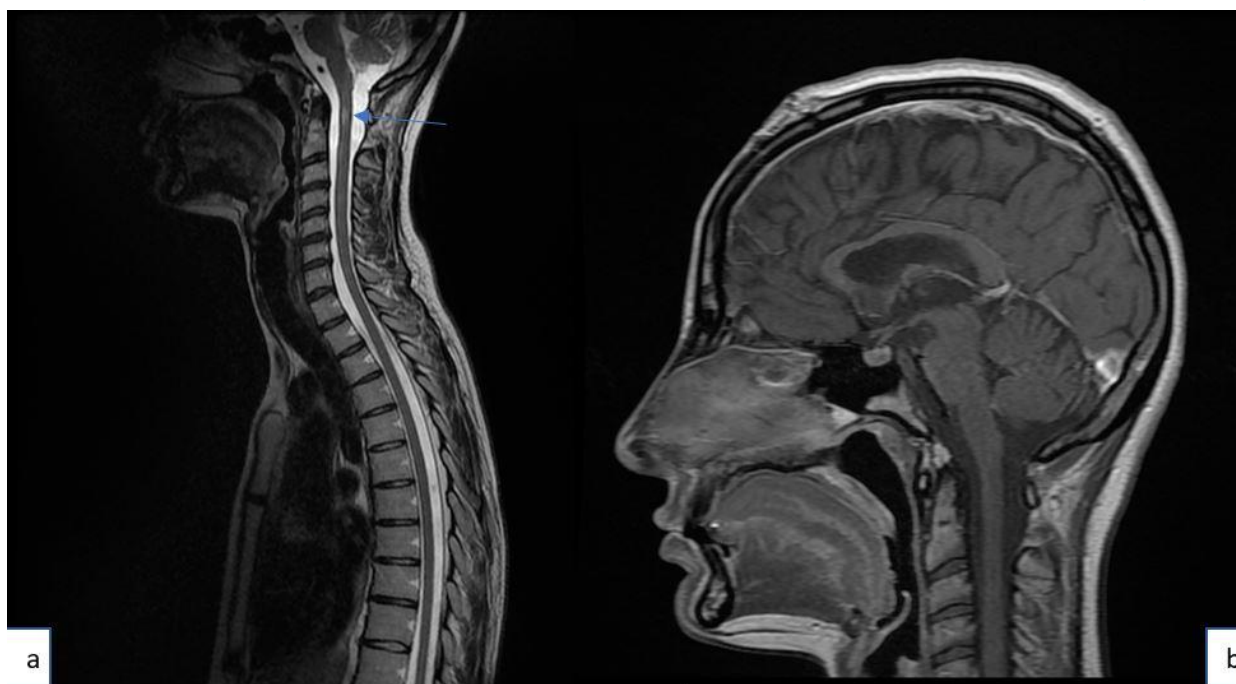
## CASE REPORT

### Case 1

A previously healthy woman of 40-year-old, 2 months after a documented COVID-19 respiratory infection that did not require a hospitalization, was admitted to the emergency department with seizures followed by coma. The symptomatology began, according to family members, a few days before when she experienced fever, headache, with a hemiparesis and behavioral changes while refusing a medical consultation. Neurological examination was difficult given the clinical state and found only a positive right Babinski's sign. Routine biochemical tests were normal. Cerebrospinal fluid (CSF) analysis showed germ-free pleocytosis. Oligoclonal band (OCB) were negative. Bacterial, fungal and viral PCR panels for Herpes Simplex Virus (HSV), Cytomegalovirus (CMV) and Epstein-Barr-Virus (EBV) were negative. SARS-COV2 PCR in CSF was also negative. Brain MRI was performed and showed multiple ovoid and round-shaped subcortical and infratentorial lesions hypointense on T1-weighted images (WI), hyperintense on T2WI and FLAIR, some of which were hyperintense on DWI but without a restriction on ADC map and discreetly showed ring enhancement at Gadolinium injection consisting with demyelinating lesions (Figure 1). MRI of the spine revealed a cervical spinal cord injury (Figure 2). The patient was placed under close monitoring and received methylprednisolone IV 1g per day for 10 days. Symptoms completely improved within 3 weeks and there were no relapses or sequelae during a one-year follow-up period.



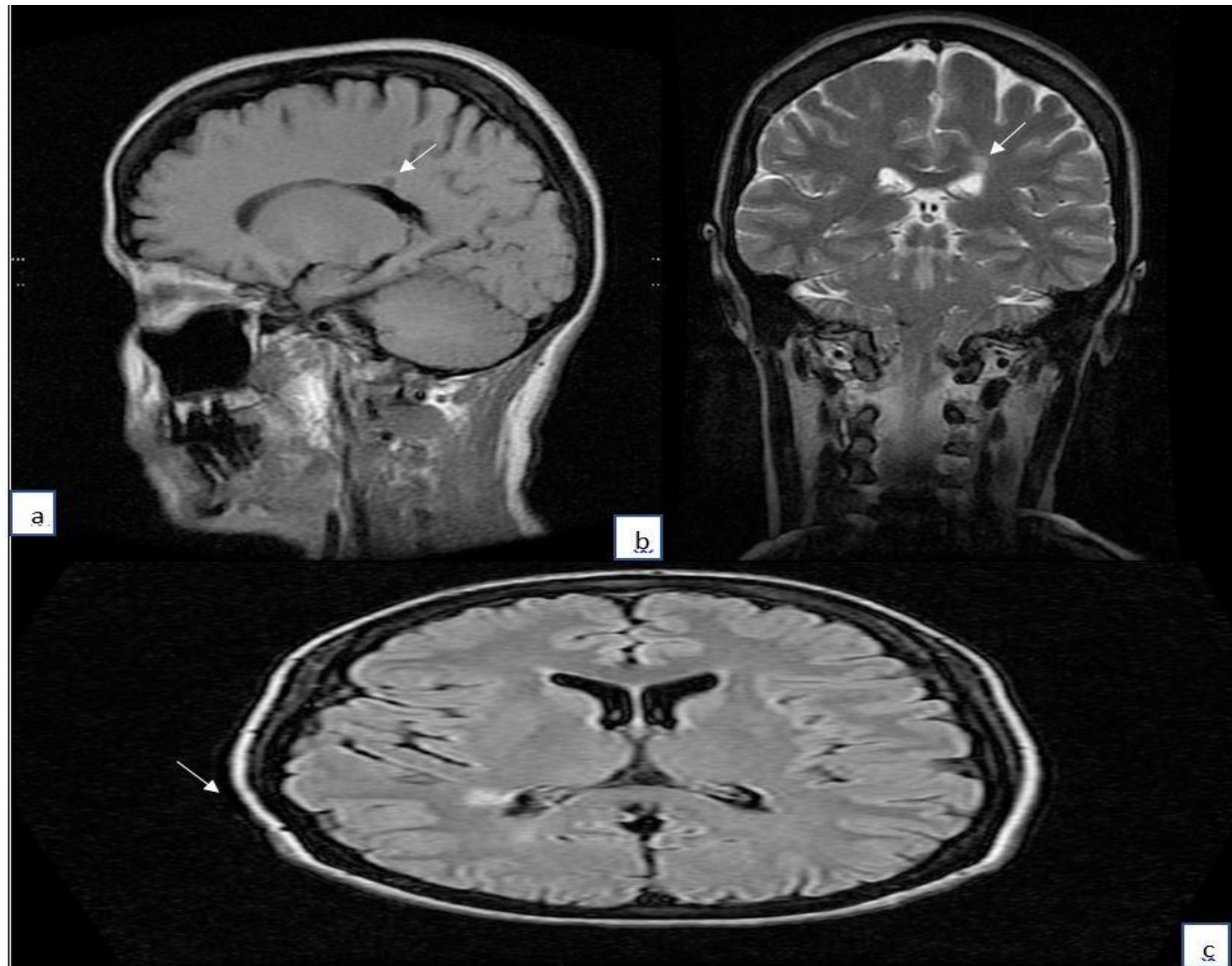
**Figure 1:** Brain MRI according to axial T2WI (a,b), axial EG(c), axial DWI (d) with ADC map (d) and coronal T1with gadolinium injection(f) sequences showing bilateral ovoid hyperintensities with no hemorrhagic feature (arrows). The lesion of the left cerebellar peduncle (arrowhead) is hyperintense on DWI with no restriction on ADC map. A subtle discreet ring enhancement of these lesions is seen (f).



**Figure 2:** Spine MRI according to sagittal T2WI (a) and T1 with Gadolinium injection sequences (b) showing a unique hyperintense cervical lesion (arrow).

### Case 2

A 46-year-old woman with no medical history, presented 3 weeks after mild respiratory COVID-19 infection a hemiparesis of the right side with no associated symptoms. Neurological examination found a 4/5 weakness with hyperexcitable deep tendons. Brain MRI revealed supratentorial periventricular lesions, hyperintense on T2WI and FLAIR without restriction on DWI or enhancement at gadolinium injection. CSF biochemical analysis was normal. Bacterial, fungal and viral screening with PCR with the available panel including that of SARS-COV2 was negative. The diagnosis of a post-COVID-19 demyelinating disease SEP-like was retained initially. Patient was made under steroids with rapid improvement and a free-relapse follow up of 18 months confirming till date that diagnosis.



**Figure 3:** Brain MRI showing a right periventricular ovoid lesion hypointense on T1WI (a), hyperintense on T2WI (b) and FLAIR (c).

## DISCUSSION

Different respiratory viruses have been documented to be neuroinvasive as influenza virus (IV), enterovirus D68 (EV-D68), the human respiratory syncytial virus (HRSV), and the human metapneumovirus (HMPV) <sup>[1,2]</sup>. The spectrum of neurological manifestations in COVID-19 range several symptoms from mild like headache, dysgeusia, anosmia to severe disorders such stroke with a variable reported frequency seen the different epidemiology of the virus around the world and the different health policies applied to face it <sup>[3,4]</sup>. Other reported manifestations included corticospinal tract signs, septic and para-infectious encephalopathy, autoimmune encephalitis like ADEM (Acute demyelinating encephalomyelitis) and GBS (Guillain Barré Syndrome). The variability of these clinical presentations led to the appearance of the accepted term of Neuro-COVID of which prevalence is still under-estimated <sup>[5,6]</sup>.

The mechanisms of neurological symptoms are still unknown with many suggested theories all of some logical reasoning. That of a direct neurological invasion is one of the main theories but not fully proven seen the negativity of RT-PCR in the CSF of many reported cases including ours <sup>[7,8]</sup>. The immune-mediated para-infectious or post-infectious theory seems stronger. Increased levels of cytokines and chemokines resulting from the hyperactivation of pro-inflammatory T cells lead to neurological damage <sup>[9-11]</sup>.

The controversies interest not only pathophysiological mechanisms but also the correlation between respiratory distress and the severity of neurological manifestations. Although it seems logical that severe symptoms like encephalopathy and acute stroke are more likely to occur in patients hospitalized with severe respiratory distress and on mechanical ventilation, in the setting of multi-organ dysfunction, some reports have denied this association <sup>[12]</sup>. Our two patients had moderate respiratory symptoms, although, they presented severe neurological syndromes several weeks after the primary infection, raising the question of the probable occurrence of a systemic inflammation and immune-mediated reaction of different expression on time and manifestations in each patient.

The certainty about imaging and its usefulness in establishing the diagnosis of respiratory infection is probably one of the few certainties of this pandemic. While chest CT has high sensitivity and relative specificity with wide availability for the diagnosis of COVID-19 <sup>[13]</sup>, precautions are needed and the need to manage these patients with non-COVID19 patients remains an issue. Brain MRI is a cornerstone in the diagnosis of neurological manifestations but with, in addition, the problem of availability and higher costs.

Radiological features are helpful in distinguishing between an ADEM-Like and a MS-Like post COVID-19, if we can use those terms. The first case would be much more ADEM-Like lesions, numerous, large, bilateral and asymmetrical, sparing the callososeptal interface. Although spinal cord involvement is rare <sup>[14]</sup>, it has been

reported and would raise the question of its frequency when SARS-COV2 is the immune mediator. The second case could be considered as a case of MS because some studies have reported the possibility of a temporal association in the 1 to 2 weeks before an infection and 3 to 5 weeks after, which is in agreement with our case <sup>[15, 16]</sup>. However, the term MS-Like would be preferable because the lesions are periventricular but not completely symmetrical and the duration of follow-up is not sufficient to validate the reality of an absence of relapse <sup>[17]</sup>.

## CONCLUSION

It is obvious that the SARS-COV2 pandemic will remain memorable for generations of the century. Many issues and questions were raised, some of which are still enigmatic. Post-COVID 19 symptoms are feared consequences and disabling neurological symptoms are high on the list of concerns, especially since humanity has not fully extricated itself from this public health issue. Research on emerging diseases must be followed to prepare the therapeutic arsenal. What is obvious and certain is that access to health care and investment in equipment as well as health personnel is a priority, because when it comes to highly contagious viruses like COVID -19, no one is safe.

## CONFLICTS OF INTEREST

Author reports no conflict of interest.

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