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POSTER PRESENTATION

Multiple sclerosis after SARS-CoV-2 infection: Causality or coincidence?

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INTRODUCTION

Since the declaration of coronavirus disease 2019 (COVID-19) pandemic in March 2020, it has become increasingly evident that several neurological complications can occur in association with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. As regards to demyelinating diseases, several cases of both central and peripheral nervous systems demyelination have been reported following COVID-19 infection. Viral infection has long been linked to the development of CNS demyelination, and this association has been reported following SARS-CoV-2 infection as well (1).

Herein, we report a case of a 36-year-old male who presented with CNS demyelinating disease, that fulfilled the diagnostic criteria of multiple sclerosis (MS), 2 months after a laboratory-confirmed infection with SARS-CoV-2.

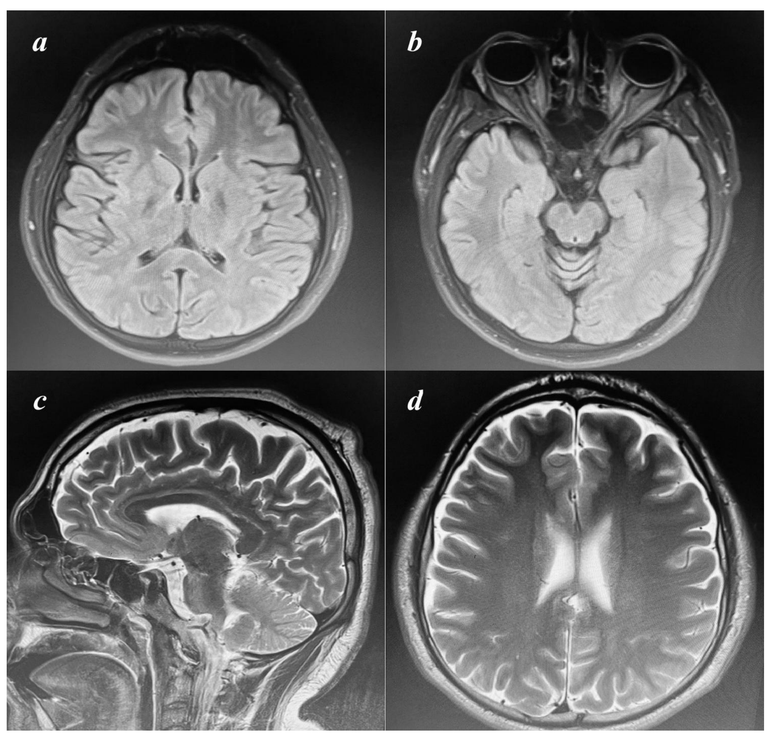
CASE PRESENTATION

A 36-year-old right handed male, with history of idiopathic generalized epilepsy since the age of 10 years, presented to our neurology outpatient clinic with unsteady gait and sense of imbalance of a one-month duration in March 2021. His epilepsy was well-controlled, and he was maintained on levetiracetam 1 gm per day. His latest magnetic resonance imaging (MRI) was in January 2020, and was normal **(Figure 1)**.

In December 2020, he developed fever, cough, generalized body pain, and he tested positive for SARS-CoV-2 via a nasopharyngeal swab reverse transcription-polymerase chain reaction (RT-PCR). He had an uncomplicated course of illness, and was managed conservatively at home. In February 2021, he started to have gait instability, recurrent falls, incoordination and dizziness, in the absence of any other cognitive, bulbar, sensory, motor or sphincteric complaint.

On examination, he was alert, conscious, and oriented with normal speech and higher mental functions. He had unsteady gait with inability for tandem walking. Cranial nerves assessment was normal, apart from bilateral gaze-evoked nystagmus. He had mild intention tremors and dysdiadochokinesia on the left side. Motor examination was of MRC grade 5/5 in both upper limbs and right lower limb, and MRC grade 4/5 in left lower limb. Deep tendon reflexes were exaggerated (3+) all over the body. Sensory assessment showed reduced superficial sensation over the left side. Planter response was mute bilaterally.

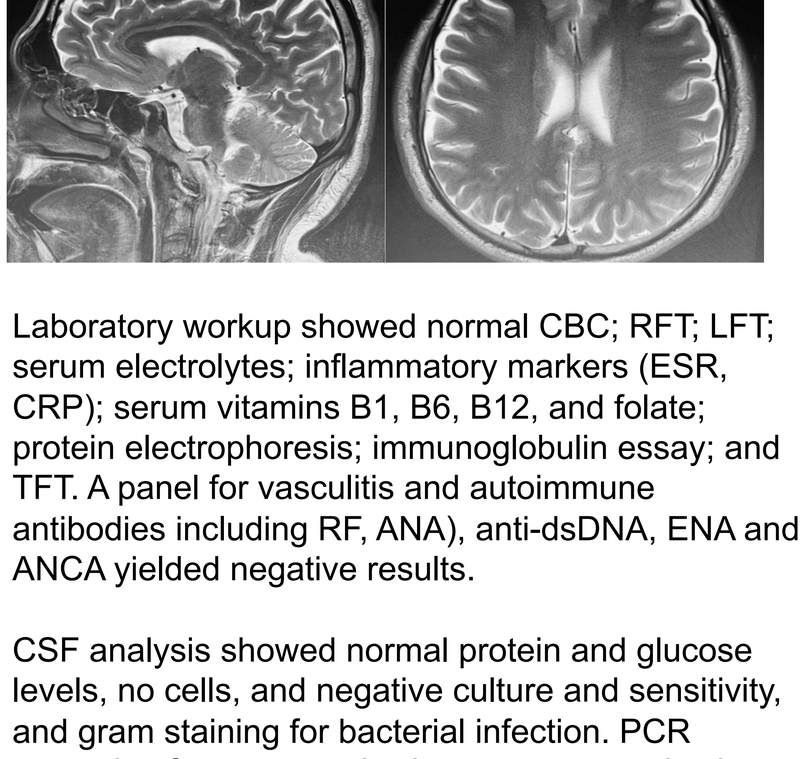
MRI of the brain with gadolinium showed multiple hyperintense white matter lesions involving the juxta-cortical and periventricular regions in both cerebral hemispheres, as well as the cerebellum, with no contrast-enhancement in any of the lesions, fulfilling the criteria of dissemination in space **(Figure 2)**.



Laboratory workup showed normal CBC; RFT; LFT; serum electrolytes; inflammatory markers (ESR, CRP); serum vitamins B1, B6, B12, and folate; protein electrophoresis; immunoglobulin essay; and TFT. A panel for vasculitis and autoimmune antibodies including RF, ANA), anti-dsDNA, ENA and ANCA yielded negative results.

CSF analysis showed normal protein and glucose levels, no cells, and negative culture and sensitivity, and gram staining for bacterial infection. PCR screening for neurotropic viruses was negative in serum and CSF.

Oligoclonal bands (OCB) were positive in CSF, fulfilling the criteria of dissemination in time. SARS-CoV-2 RNA was not tested in the CSF in our case due to delayed presentation.



The patient was commenced on intravenous methylprednisolone 1000 mg per day for 3 days, with improvement regarding the gait, and limb weakness. The patient fulfilled the revised 2017 McDonald diagnostic criteria for multiple sclerosis (MS), and he was started on fingolimod 0.5 mg per day, as a disease-modifying therapy.

DISCUSSION

To our knowledge, this is the second case report, and the first from Middle East and North Africa (MENA) region. The concept of "*no better explanation*" posed a diagnostic challenge in such cases. MS pathogenesis could have been triggered by SARS-CoV-2, or this could be an exacerbation of a predetermined MS.

It has been demonstrated that viral infection can induce an inflammatory response, activating myelin-specific T cells, which can accelerate the development of early or delayed virus-induced demyelination. Historically, SARS-CoV and MERS-CoV, which are genetically similar to SARS-CoV-2, has been associated with central demyelination in literature (2).

SARS-CoV-2 exhibits neurotropic properties and can cause direct neurological damage, through binding to angiotensin-converting enzyme-2 (ACE-2) receptors in CNS, or via blood circulation. Moreover, delayed CNS damage appears to be mediated by an undesired immune reaction, leading to acute or delayed CNS demyelination.

Accumulated evidence showed that SARS-CoV-2 and several proinflammatory cytokines, including IL-2, IL-4, IL-6, IL-8, IL-10, TNF-α, and IFN-γ, can cross the blood-brain-barrier, infecting macrophages, microglia, and astrocytes, which are the principal cells that mediate innate immunity in the CNS, thus creating a "perfect storm" for a pro-inflammatory state.

IL-6 is an important pro-inflammatory mediator that can induce an immune response in the nervous system, and plays a crucial role in regulating the immune response in MS. The levels of IL-6 were found to be correlated with the severity of COVID-19 symptoms, and this dysregulation can affect both innate and acquired immunity. Furthermore, most COVID-19 patients exhibit increased circulating levels of IL-17, which has a documented role in MS pathogenesis, based on the data from EAE model. In addition, Toll-like receptors (TLR), the main pattern recognition receptors in CNS, have played a significant role in the pathogenesis of both MS and COVID-19 (3).

A possible alternative explanation could be the production of antibodies against myelin triggered by the virus. This para-infectious or post-infectious etiology is reported in several cases of post-SARS-CoV-2 Guillain-Barre syndrome. SARS-CoV-2 may play a role in triggering MS, similar to the documented role of EBV (4).

CONCLUSIONS

We report a case of CNS demyelination following COVID-19 infection, that fulfilled the diagnostic criteria of MS. Our case adds to the growing field of research on the influence of SARS-CoV-2 on the nervous system, potentially triggering demyelination through an autoimmune CNS inflammatory process. Clinical and radiological monitoring is recommended in such cases, as the course of the demyelinating disease still seems unpredictable.

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