

Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active. Contents lists available at ScienceDirect



Multiple Sclerosis and Related Disorders

journal homepage: www.elsevier.com/locate/msard



Correspondence

COVID-19 in a temporal relation to the onset of multiple sclerosis

Check for updates	

ARTICLE INFO	A B S T R A C T
Keywords Multiple sclerosis Coronavirus SARS-CoV-2 COVID-19 Anosmia	Neurological complications of COVID-19 have been described. We present the case of a 27-year-old woman who developed COVID-19 in April 2020. She continued to present anosmia and ageusia eight months later. Six months after contracting COVID-19, she developed dysesthesia, hypoesthesia and hyperreflexia. Her magnetic resonance imaging showed demyelinating lesions, of which two were enhanced by gadolinium. She was positive for oligoclonal bands in her spinal fluid. This patient developed multiple sclerosis with a temporal relationship to COVID-19. We believe that SARS-CoV-2 led to her autoimmune disease through a virus-induced neuro-immunopathological condition.

1. Introduction

In December 2019, the first case of a new human coronavirus infection (SARS-CoV-2; COVID-19) was reported in Wuhan, China. One year later, it has now caused an unprecedented pandemic with more than 73 million confirmed cases including 1.6 million deaths (WHO Coronavirus Disease (COVID-19), 2020). COVID-19 infection mainly affects the respiratory system but it has also shown manifestations and complications in multiple organs (Montalvan et al., 2020; Palao et al., 2020).

Numerous studies have presented evidence of neurological symptoms associated with COVID-19, including headache, anosmia and hypogeusia. Serious manifestations have been observed, like acute cerebrovascular diseases, impaired consciousness and skeletal muscle injury (Montalvan et al., 2020; Palao et al., 2020). However, the information available on demyelinating diseases triggered by COVID-19 remains limited. Only one case of optic neuritis, diagnosed after SARS-CoV-2 infection had been detected, has been reported (Mao et al., 2020). Although that case fulfilled the diagnostic criteria for multiple sclerosis, no gadolinium-enhancing lesions were observed. Therefore, the authors of that case presumed that the pathogenic process had started before the viral infection, and that the virus might have acted as a precipitating factor. Given the uncertainty of the current evidence, it is important to investigate the possibility of this association.

2. Case report

The present report was approved by the Ethics Committee at Universidade Metropolitana de Santos and a written consent statement was signed by the patient.

We report the case of a 27-year-old Caucasian woman who developed COVID-19 in April 2020. Her main symptoms were high temperature, dry cough, anosmia and hypogeusia. Other family members also developed COVID-19 at that time and recovered soon, but the patient reported here continued to present anosmia and ageusia eight months later. Her olfactory bulbs evolved with atrophy, as seen in recent magnetic resonance imaging (MRI) (Fig. 1). No neurological examination was performed at this time.

Six months after contracting COVID-19, the patient developed a feeling that her left arm was different, like "being cold from inside". This symptom progressed and came to affect both left limbs and the left side of the thoracic region. She was initially diagnosed as presenting "anxiety", but the symptoms continued and, two months later, she came for a neurological consultation.

Her examination confirmed the presence of anosmia, hypoesthesia in the left limbs and left side of the thorax, and global deep tendon hyperreflexia with bilateral Babinski sign. Her magnetic resonance imaging (MRI) showed two gadolinium-enhancing lesions (frontal lobe and cervical spinal cord) and three other periventricular encephalic lesions. There were clear signs of a central vein inside the demyelinating lesions. Fig. 1 shows the demyelinating lesions in MRI and the persistent lesions in both olfactory bulbs. The patient's spinal fluid was positive for oligoclonal bands and had negative PCR for SARS-Co/v2. This case fulfilled the diagnostic criteria for multiple sclerosis (MS) (Thompson et al., 2018).

- A Hyperintense lesion in the right corona radiata, in axial T2-FLAIR.
- B Susceptibility-weighted imaging (SWI) showing a periventricular longitudinal central vein in a demyelinating lesion in the right corona radiata. The central vein sign is a marker for multiple sclerosis (9).
- C Demyelinating lesions perpendicular to the right lateral ventricle, in axial T2-FLAIR.
- D Juxtacortical lesion identified in the left superior frontal gyrus, in axial T2-FLAIR.
- E Short-tau inversion recovery (STIR) imaging in sagittal T1, showing a hyperintense lesion at C2-C3 level.
- F Axial T1 of the cervical spinal cord, showing a gadolinium-enhancing lesion in the lateral funiculus at C2-C3 level.
- G Sagittal T1 with fat saturation, showing hyperintensity in the right olfactory bulb.
- H Coronal T1, showing thinning of the olfactory bulbs.

https://doi.org/10.1016/j.msard.2021.102863

Received 7 January 2021; Received in revised form 21 February 2021; Accepted 22 February 2021 Available online 24 February 2021 2211-0348/© 2021 Elsevier B.V. All rights reserved.



Fig. 1. Magnetic resonance imaging of the patient two months after onset of multiple sclerosis symptoms.

A- Hyperintense lesion in the right corona radiata, in axial T2-FLAIR.

B- Susceptibility-weighted imaging (SWI) showing a periventricular longitudinal *central vein in a demyelinating lesion in the right corona radiata. The central vein sign* is a marker for multiple sclerosis (9).

- C- Demyelinating lesions perpendicular to the right lateral ventricle, in axial T2-FLAIR.
- D- Juxtacortical lesion identified in the left superior frontal gyrus, in axial T2-FLAIR.
- E- Short-tau inversion recovery (STIR) imaging in sagittal T1, showing a hyperintense lesion at C2-C3 level.
- F- Axial T1 of the cervical spinal cord, showing a gadolinium-enhancing lesion in the lateral funiculus at C2-C3 level.
- G- Sagittal T1 with fat saturation, showing hyperintensity in the right olfactory bulb.
- H- Coronal T1, showing thinning of the olfactory bulbs.

3. Discussion

While an association between COVID-19 and MS does not necessarily signify causation, the temporal relationship between these two events and the potential SARS-CoV-2 neurotropism suggest that our patient had a virus-induced neuroimmunopathological condition.

Focal demyelination is unlikely to have been the result of direct infection by the virus in this case. Presence of SARS-CoV-2 could have led to activation of T-lymphocytes, which would be responsible for the demyelination and activation of the microglia and inflammatory mediators (Savarin and Bergmann, 2017). In addition, the persistent anosmia was associated with abnormal enhancement on MRI. A similar event had previously been reported by Aragão et al (Aragão et al., 2020).

Although the authors are fully aware of the possible coincidence in this anecdotal case, MS may be an extra possible neurological complication of COVID-19. Over time and with further observations this question may be answered.

Funding

None

Declaration of Competing Interest

None

References

Aragão, M., Leal, M.C., Cartaxo Filho, O.Q., Fonseca, T.M., Valença, M.M., 2020. Anosmia in COVID-19 associated with injury to the olfactory bulbs evident on MRI. AJNR Am. J. Neuroradiol. 41 (9), 1703–1706. https://doi.org/10.3174/ajnr.A6675.

- Mao, L., Jin, H., Wang, M., et al., 2020. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. JAMA Neurol. 77 (6), 683–690. https://doi.org/10.1001/jamaneurol.2020.1127.
- Montalvan, V., Lee, J., Bueso, T., et al., 2020. Neurological manifestations of COVID-19 and other coronavirus infections: a systematic review. Clin. Neurol. Neurosurg. 194, 105921 https://doi.org/10.1016/j.clineuro.2020.105921.
- Palao, M., Fernández-Díaz, E., Gracia-Gil, J., et al., 2020. Multiple sclerosis following SARS-CoV-2 infection. Mult. Scler. Relat. Disord. 45, 102377 https://doi.org/ 10.1016/j.msard.2020.102377.
- Savarin, C., Bergmann, C.C., 2017. Viral-induced suppression of self-reactive T cells: lessons from neurotropic coronavirus-induced demyelination. J. Neuroimmunol. 308, 12–16. https://doi.org/10.1016/j.jneuroim.2017.01.003.
- Thompson, A.J., Banwell, B.L., Barkhof, F., et al., 2018. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. Lancet Neurol. 17 (2), 162–173. https:// doi.org/10.1016/S1474-4422(17)30470-2.
- WHO Coronavirus Disease (COVID-19) Dashboard. https://covid19.who.int/. Accessed on 19 December 2020. 2.

Yara D. Fragoso^{a,b,*}, Filippe A.S. Pacheco^{C,e}, Guilherme L. Silveira^d, Rodrigo A. Oliveira^d, Vitor M. Carvalho^{b,e}, Ana Luiza C. Martimbianco^a ^a Professor of the Postgraduate Program for Health and Environment,

- Universidade Metropolitana de Santos, Santos, SP, Brazil
 - ^b MS & Headache Research, Santos, SP, Brazil
 - ^c Filippe Pacheco Clinic, Santos, SP, Brazil
 - ^d Mega Imagem, Santos, SP, Brazil

^e Postgraduate Program for Health and Environment, Universidade Metropolitana de Santos, Santos, SP, Brazil

^{*} Corresponding author at: Department of Neurology, Medical School, UNIMES, Avenida Conselheiro Nebias 536, Santos, SP CEP 11045-002, Brazil.

E-mail address: yara@bsnet.com.br (Y.D. Fragoso).