CASO CLÍNICO/CASE REPORT

Post-COVID-19 Myelitis Manifesting as Partial Brown-Séquard Syndrome

Mielite Pós-COVID-19 Apresentando-se como Síndrome de Brown-Séquard Parcial

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Abstract

Myelitis is a rare neurological complication of COVID-19. We will describe a patient with post-COVID-19 myelitis manifesting as partial Brown-Séquard syndrome.

A 33-year-old male presented with progressive weakness of the lower limbs, evolving over the previous week. Six weeks before, the patient had had COVID-19, from which he had already recovered. Neurological examination revealed right lower limb weakness and reduced pain sensation on the left lower limb, with a T5-T6 sensory level. Thoracic magnetic resonance imaging (MRI) revealed a right intra-medullary lesion spanning from T3 to T4 with T2 signal hyperintensity. Cerebrospinal fluid study was normal, and SARS-CoV-2 was undetected. After excluding active infection, the patient received methylprednisolone and the symptoms improved. One month later, the neurological exam was considered normal and there was a significant lesion reduction on MRI.

SARS-CoV-2 infection should be considered as a possible aetiology for myelitis in all patients, even in those with mild infection or asymptomatic.

Resumo

A mielite é uma complicação neurológica rara da COVID-19. Descrevemos o caso de um doente com mielite pós-COVID-19, que se apresenta como síndrome de Brown-Séquard parcial.

Um doente do sexo masculino, 33 anos, recorre ao hospital por história de fraqueza progressiva dos membros inferiores com uma semana de evolução. Seis semanas antes, tinha tido COVID-19, entretanto recuperado. Ao exame neurológico, apresentava défice de força do membro inferior direito e hipostesia à esquerda, com nível sensitivo T5-T6. A ressonância magnética (RM) torácica revelou lesão intramedular hiperintensa direita em T3-T4. O estudo do líquido cefalorraquidiano foi normal e não foi detetado SARS-CoV-2. Após exclusão de infeção ativa, o doente iniciou metilprednisolona, observando-se melhoria clínica. Um mês depois, o exame neurológico era normal e houve marcada redução da lesão na RM.

A infeção por SARS-CoV-2 deve ser considerada como uma possível etiologia de mielite em todos os doentes, mesmo naqueles com infeção ligeira ou assintomáticos.

Introduction

Coronavirus disease (COVID-19) is the largest and most severe pandemic of our day.[1,2]

Although severe neurological complications are rare, the scale of the current pandemic translates into a significant pool of cases. They can be considered as para-infectious or post-infectious immune-mediated diseases.[1,2]

Myelitis has been described most frequently as a post-infection complication and appears to be severe and with great impact in the recovery.[1,2]

We describe a patient with post-COVID-19 myelitis manifesting as a partial Brown-Séquard syndrome.

Case Report

A 33-year-old male with unremarkable previous medical history presented with a one-week history of progressive weakness, diminished sensation in the lower limbs and urinary hesitancy. Six weeks before, the patient had been diagnosed with COVID-19, with a fever and mild respiratory symptoms. SARS-CoV-2 RNA was detected on a nasopharyngeal swab by a reverse transcription-polymerase chain reaction (RT-PCR) method. He fully recovered and became SARS-CoV-2 negative after 3 weeks. The patient had not been vaccinated against SARS-CoV-2 at that time.

Neurological examination revealed right lower limb weakness (grade 4/5), left-sided hemihypoesthesia below T5-T6 and a hyperesthesic area coincident with the right T4 dermatome. Vibratory and joint position sensations were normal. Cognition and cranial nerves were unaffected.

Spinal cord magnetic resonance imaging (MRI) revealed a T2 hyperintense intra-medullary lesion spanning from T3 to T4, located at the right anterolateral region, with gadolinium enhancement (**Fig.s 1** and **2**). Brain MRI was normal. Neuro-ophthalmologic evaluation, including optical coherence tomography and visual evoked potentials were normal, excluding subclinical damage of optic nerves.

General blood tests were unremarkable, including leucocytes, erythrocyte sedimentation rate, C-reactive protein, angiotensin converting enzyme, adenosine deaminase, folate, vitamin B12, 25-hydroxyvitamin D and protein electrophoresis. Serology (IgG) for SARS-CoV-2 was positive (IgM negative). Serology for Epstein-Barr virus was positive, with a pattern indicating a past infection. Serologies for cytomegalovirus, herpes simplex virus 1 and 2 (HSV 1 and 2), syphilis, brucella, borrelia, varicella-zoster, mycoplasma, interferon gamma

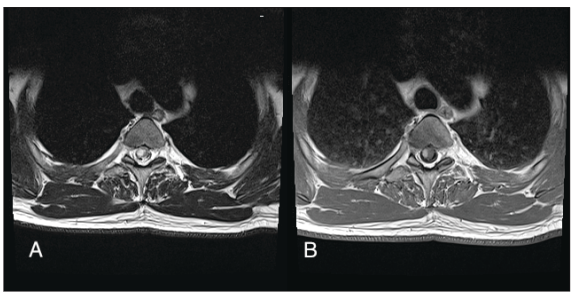

Figure 1. Pre-treatment spinal cord MRI. Axial T2-weighted (A) and T1 gadolinium (B) images show signal hyperintensity at the right anterolateral region of the spinal cord with lesion enhancement.

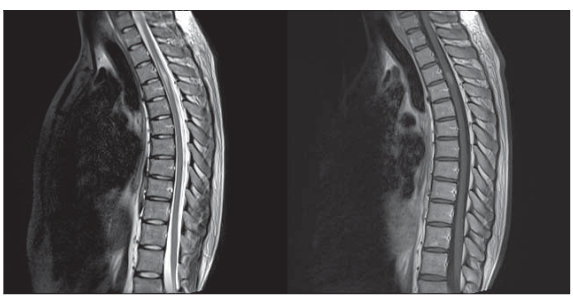

Figure 2. Pre-treatment spinal cord MRI. Sagittal T2-weighted (A) and T1 gadolinium (B) images show signal hyperintensity spanning from T3 to T4 with lesion enhancement.

and HIV were negative. The autoimmune panel, including antinuclear antibodies, anti-double stranded DNA, extractable nuclear antigen antibodies (anti-SS-A, anti-SS-B, anti-RNP, anti-Jo-1, anti-Sm and anti-Scl70), anti-neutrophil cytoplasmic antibodies, cardiolipin antibodies and beta-2 glycoprotein I antibodies was normal. Antibodies for myelin oligodendrocyte glycoprotein and aquaporin 4 were negative.

Cerebrospinal fluid (CSF) study was normal (protein 22 mg/dL, glucose 63 mg/dL, cell count 1/mm^3). Multiplex-PCR detection for HSV-1, HSV-2, enterovirus, varicella-zoster virus, human herpesvirus 6, human parechovirus, cytomegalovirus, *Neisseria meningitidis*, *Streptococcus pneumoniae*, *Escherichia coli*, *Streptococcus monocytogenes* and *cryptococcus neoformans/gattii* was negative. CSF cultures for bacteria, viruses, and fungi were negative. IgG oligoclonal bands were negative and SARS-CoV-2 RNA was not detected by RT-PCR.

After excluding active infection, the patient was started on methylprednisolone (1 g/daily for 5 days) with a rapid improvement of the symptoms, being discharged on a tapering regimen of oral steroids.

One month later, the patient was asymptomatic, the neurological exam was normal, and the spinal cord MRI showed a considerable reduction of the lesion volume

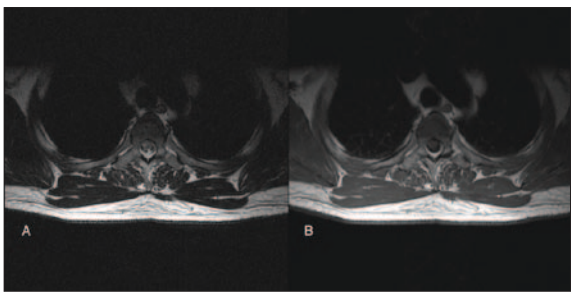

Figure 3. Post-treatment spinal cord MRI. Axial T2-weighted (A) and T1 gadolinium (B) images show marked improvement of the spinal cord lesion.

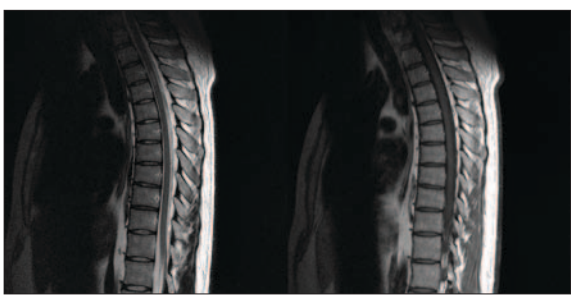

Figure 4. Post-treatment spinal cord MRI. Sagittal T2-weighted (A) and T1 gadolinium (B) images show marked improvement of the spinal cord lesion, with no evidence of enhancement.

without gadolinium enhancement (**Fig.s 3** and **4**). One year later, the patient remains asymptomatic, with no signs of infectious or demyelinating disease.

Discussion

Recognition of neurological disease associated with SARS-CoV-2 in patients whose respiratory infection is mild or asymptomatic might prove challenging, especially if COVID-19 illness occurred weeks earlier. Other authors have suggested criteria for the definition of COVID-19-related neurological disease, namely the presence of SARS-CoV-2 in respiratory or other non-CNS samples, thus indicating acute infection at the time of neurological symptoms onset. A time frame of 6 weeks has been suggested for Guillain-Barré syndrome, however this time period has not been defined for myelitis.[1] In spite of this, most of the published cases of myelitis related to SARS-CoV-2 had a latency period ranging from 10 days to 6 weeks, suggesting a post-infectious origin.[3,4]

It is known that SARS-CoV-2 is a neurotropic virus, but the disease mechanisms are not yet fully understood.[1,2] The angiotensin converting enzyme 2 receptor, essential for the virus to enter cells, is also found in brain vascular endothelium and one of the possible entry routes to the central nervous system (CNS) is through the olfactory bulb.[1,2] The neurological disease mechanisms include direct viral invasion, a systemic inflammatory response and a prothrombotic state.[1,2] Several mechanisms have been proposed for post-infectious neurological disorders, such as molecular mimicry (the self-antigen has a similar structure to the pathogen-antigen, resulting in loss of immune tolerance), epitope spreading (there is a widening immune response to other epitopes, including self-antigens), bystander activation (immune cells produce inflammatory mediators, which can activate autoreactive lymphocytes) and polyclonal B-cell activation caused by persistent infection.[1-4]

In this case, direct infection of the CNS by SARS-CoV-2 seems unlikely since the myelitis occurred six weeks after the acute infection and the virus was not detected in the CSF by RT-PCR. Therefore, we assumed the diagnosis of post-infectious myelitis secondary to SARS-CoV-2 infection, considering the temporal profile, the exclusion of other causes after an extensive workup and the evident clinical improvement that occurred after steroid treatment.

To the best of our knowledge, only a few cases of myelitis as a complication of COVID-19 have been reported,[3,5-9] with an estimated incidence of 0.5 per million.[3] Most of the cases were in middle aged men, manifesting as acute transverse myelitis and tetraparesis.[3,5-9] Despite longitudinally-extensive lesions being the most prevalent, 30% of the cases affected 3 or less cord segments, mostly at thoracic levels.[3] Most of the reported cases had a long latency period (>10 days), however only 2 cases were reported after 4 weeks of COVID-19 infection.[3] CSF examinations revealed inflammatory changes on several cases, but only two patients tested positive for SARS-CoV-2 in the CSF.[3,8] Most of them were treated with steroids, but the overall response to treatment was unsatisfactory.[3,5-8] Our case sets itself apart from others because it manifested as a short myelitis lesion 6 weeks after COVID-19 infection, in a younger individual, with an excellent response to steroids and full recovery.

More neurological complications are expected to arise in clinical practice and, therefore, a higher level of suspicion for SARS-CoV-2 association is needed, even if the symptoms appear weeks after COVID-19 and the patients had mild or asymptomatic infection. Testing for SARS-CoV-2 on CSF should be incorporated in the diagnostic workup of an inflammatory myelitis. To hasten recovery, prompt treatment with high-dose intravenous steroids should be initiated. ■

Contributorship Statement / Declaração de Contribuição

CS: Concepção; análise e interpretação dos dados; Redação e aprovação final.

ACL: Concepção; Redação e aprovação final.

IS: Revisão crítica com contribuição intelectual; Aprovação final.

SB: Concepção; análise e interpretação dos dados; Redação e revisão crítica; Aprovação final.

Responsabilidades Éticas

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