Longitudinally Extensive Transverse Myelitis (LETM) in COVID-19 Infection, A Case-Report

Jean-Christophe Van Cutsem (jcvanc@hotmail.com)
Ghent University: Universiteit Gent https://orcid.org/0000-0002-5537-6422
Ann-Sophie Lamon
Ghent University: Universiteit Gent
Vincent Van Belleghem
Algemeen Ziekenhuis Groeninge: AZ Groeninge
Evelien Vancaester
AZ Groeninge - Campus Kennedylaan: AZ Groeninge

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Abstract

Introduction

Since the COVID-19 pandemic, a growing number of central nervous system (CNS) complications in patients with COVID-19 have been reported. Isolated, longitudinally extensive transverse myelitis (LETM), is a unique presentation of CNS involvement. The limited reports, its diverse clinical manifestations and the possible long-term consequences make the reporting crucial to further our understanding of those syndromes occurring in COVID-19 positive patients.

Case Presentation

A 63-year old male consulted the emergency department after a sudden onset of gait ataxia, a one-week history of paresthesia progressing from the feet to the midsternal area and urinary. He tested positive on a SARS-CoV-2 RNA RT-PCR nasopharyngeal swab two days prior to the onset of his symptoms. Neurological examination showed a sensory level at T7 with symmetrically reduced fine touch, vibration, proprioception and furthermore an ataxic gait was observed. Cerebrospinal fluid on day one of admission showed pleocytosis, predominantly neutrophils, elevated protein count and normal glucose level and IgG. MRI of the spinal cord revealed a diffusely increased signal intensity involving the near-complete spinal cord, from the brainstem to level T12, fitting the diagnosis of LETM.

Conclusion

The few cases of transverse myelitis in association with COVID-infection are believed to have an immune-mediated postinfectious mechanism. In this case however, parainfectious direct viral invasion of the spinal cord is far more likely because of a neutrophilic predominance in CSF and a short timespan between infection and symptoms. It could provide more clues that the SARS-CoV-2 is acutally capable of causing direct neurotoxic effects.

Introduction

Since the COVID-19 pandemic, a growing number of central nervous system (CNS) complications in patients with COVID-19 have been reported. A minority consists of inflammatory syndromes such as meningoencephalitis, Guillain-Barre syndrome (GBS), acute disseminated encephalomyelitis (ADEM) and myelitis. Isolated, longitudinally extensive transverse myelitis (LETM), is one of the more unique presentations of CNS involvement. LETM is defined as a transverse myelitis which extends over a continuous lesion which is at least 3 vertebral segments in length on radiologic findings [1]. The limited reports, its diverse clinical manifestations and the possible long-term consequences make the reporting crucial to further our understanding of those syndromes occurring in COVID-19 positive patients and to provide evidence based guidelines for management and treatment.

Case Presentation

A 63-year old male consulted the emergency department of Courtrai, Belgium, after a sudden onset of gait ataxia. He further complained of a one-week history of paresthesia progressing from the feet to the midsternal area, thoracolumbar back pain as well as urinary hesitancy leading to urinary retention on day 2 of hospital admission. The patient had a history of atrial fibrillation, coronary artery disease and depression. He tested positive on a SARS-CoV-2 RNA RT-PCR nasopharyngeal swab two days prior to the onset of his symptoms. The man was tested after a high-risk contact with a COVID-19 positive person, but never experienced respiratory or infectious symptoms.

Neurological examination showed a sensory level at T7 with symmetrically reduced fine touch, vibration, proprioception and furthermore an ataxic gait was observed. There were no signs of muscle weakness. Deep tendon reflexes of the lower limbs were brisk with up-going plantar reflexes and clonus.

The next day, initially observed ankle reflexes and clonus were absent and patellar reflex appeared weak. The second day he experienced a slight loss of strength in the lower limbs and urinary retention.

Cerebrospinal fluid on day one of admission showed pleocytosis (455/µL), predominantly neutrophils, elevated protein count (622 mg/L) and normal glucose level and IgG. Blood analysis revealed a mildly elevated C-reactive protein (CRP) (20.5mg/L) and D-dimer (869µg/L). No further significant biochemical abnormalities were seen.

Extensive screening on serum including HIV I and II, hepatitis B, hepatitis C, Human T-lymphotropic virus 1 and 2, Syphilis (VDRL and TPPA), Brucella and quantiferon test for Mycobacterium tuberculosis was negative, as were cultures on blood and CSF.

After positive immunoglobulin G (IgG) for Borrelia burgdorferi was observed in serum, IgG index in CSF was determined and concluded no arguments for neuroborreliosis.

Angiotensin-converting enzyme (ACE), antibodies for aquaporin-4 (AQP4) and myelin oligodendrocyte glycoprotein (MOG) in serum were negative. Autoimmune and paraneoplastic panels did not indicate an underlying condition.

Screening on CSF for endemic neurotropic pathogens, including Herpes Simplex 1 and 2, Haemophilus Influenzae, Cytomegalovirus, Human Herpesvirus 6, Varicella Zoster virus, Listeria monocytogenes, etc. was negative. No oligoclonal bands (OCB) were detected.

CSF PCR for COVID-19 virus was tested negative at day 1 and day 6 of hospitalisation.

MRI of the spinal cord revealed a diffusely increased signal intensity involving the near-complete spinal cord, from the brainstem to level T12, fitting the diagnosis of LETM (Fig. 1). Brain MRI was normal.

Initially empirical treatment with intravenous acyclovir was started. After the serum and CSF analysis were negative, this was discontinued and corticosteroid therapy was administered.

After two weeks, the patient could be transferred to the rehabilitation department. At discharge the patient reported reduced back pain and paresthesia. The strength in the lower limbs was improved, though walking remained impossible due to severe ataxia.

In our case we noticed an aberrant course of the deep tendon reflexes, which started with signs of spasticity at admission, and evolved to a hyporeflexia the next day. Along with the increasing weakness and urinary retention, this was considered as disease progression which led to the emergence of spinal shock.

Conclusions

Most cases of transverse myelitis in association with COVID-infection are believed to have an immune-mediated postinfectious mechanism. Though in this case parainfectious direct viral invasion of the spinal cord is likely. [2]. There is a short time span between the time of infection and the onset of symptoms. For this patient, the time span is particularly well documented, in contrast with most cases related to asymptomatic COVID-infection. The patient tested positive two days prior to the onset of symptoms, five days after a high-risk contact. On the first day of his high-risk contact he was tested negative. This temporal relationship advocates more to a direct infectious mechanism which makes this, to the best of our knowledge, one of four cases reported [1].

Those few cases of COVID-related LETM, except one [1], showed a CSF lymphomonocytosis, whereas in this case neutrophils were predominant. A second lumbar puncture was done after six days, which showed a shift to lymphocytosis. Molecular mimicry and bystander activation seem to be responsible for the post-infectious, auto-immune mediated SARS-CoV-2-associated ATM. They are both lymphocyte-mediated mechanisms. As such, CSF with neutrophilic predominance as described in this case, could be another clue to the direct viral neurotropism effects. Interestingly, the only other case found in literature with neutrophilic predominance in a COVID-19 related LETM, also described a short timespan between infection and symptoms and was also considered to have a para-infectious mechanism with direct viral neurotropism [1].

It is hypothesized that with this mechanism, the virus first penetrates the CNS through a hematogenous route after the disruption of the blood-brain barrier or through transneuronal spread from the olfactory, trigeminal or vagus nerve. Viral replication in the brain cells, injury to immune cells and misdirected immune response of the host can all lead to direct neurotoxic effects [3].

Although CSF PCR for COVID-19 virus was tested negative at day 1 and day 6 of hospitalisation, a direct infectious mechanism cannot be excluded. It is believed that the virus spreads transiently in the CSF and titers are extremely low [4]. This could also explain why only a handful of cases reported a positive PCR in CSF. [1].

Nevertheless, the number of patients with COVID-19-associeted myelitis remains small. Further data and research is needed to distinguish between infectious and postinfectious mechanisms.

Declarations

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Conflicts of interest: *The authors declare that they have no conflict of interest.*

Availability of data and material (data transparency): *'Not applicable'*

Code availability (software application or custom code): *'Not applicable'*

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Ethics approval (include appropriate approvals or waivers)*: 'Not applicable'*

Consent to participate*:* Informed consent was obtained from the participant included in the study.

Consent for publication: The participant has consented to the submission of the case report to the journal.

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Figures

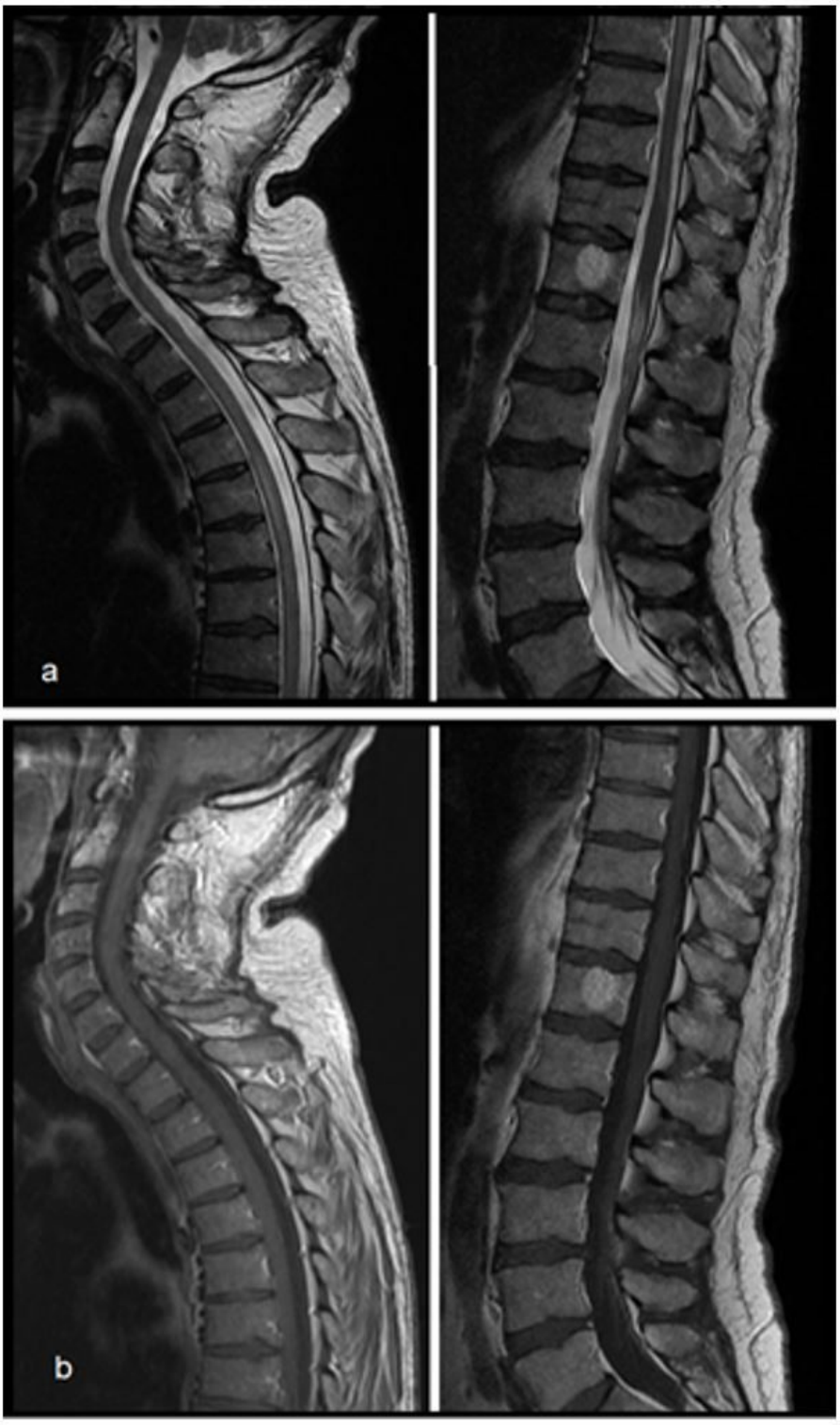

Figure 1

MRI of the spinal cord. (a) T2-weighted sagittal view of the cervicothoracic (left) and lumbar (right) spinal cord, demonstrating diffuse extensive hyperintensities. (b) Sagittal T1 Gadolinium enhanced images showing no evidence of enhancement.

Supplementary Files

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- Carechecklist.pdf