

Transverse Myelitis after COVID-19 Disease: A Case Report

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Summary. Currently, a significant number of post-COVID-19 disease neurological disorders still occur, and precise analysis of them could expand the knowledge of the neurological community for future pandemics. It is important to evaluate and recognize potential neurological manifestations and complications of COVID-19, as some of them can progress rapidly and require urgent treatment.

We present a clinical case of transverse myelitis after a COVID-19 in a 35-year-old man who was treated at the Neurology Department of the Hospital of Lithuanian University of Health Sciences Kaunas Clinics.

Keywords: transverse myelitis, COVID-19.

INTRODUCTION

Acute idiopathic inflammatory myelitis is an inflammatory injury of the spinal cord that causes a well-recognized clinical syndrome. It often presents with a rapid onset weakness, sensory deficits, and bowel or/and bladder dysfunction [1]. Its pathogenesis consists of direct virus damage, impairment caused by cytokine hyperproduction, and molecular mimicry between the virus and myelin which causes sensitization of the immune system to neurons antigens. All this leads to damage to myelin and axons [2].

Currently, a significant number of post-COVID-19 neurological disorders still occur, and precise analysis of them could expand the knowledge of the neurological community for future pandemics. It is important to evaluate and recognize potential neurological manifestations and complications of COVID-19, as some of them can progress rapidly and require urgent treatment.

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CASE REPORT

On April 7, 2021, a 35-year-old man arrived at the Emergency Department (ER) of the Hospital of Lithuanian University of Health Sciences Kaunas Clinics with complaints of numbness in his legs and aggravated urination and defecation. From March 20, 2021, he was isolated at home with his wife who had severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. The patient experienced commonly described symptoms of COVID-19 disease: smell impairment, fever, and other flu-like symptoms, so polymerase chain reaction (PCR) test for the virus was not performed and the diagnosis, according to epidemiological data at that time, seemed clear. For clarity, it should be noted here that the patient later did anti-SARS-CoV-2 IgG blood test and its count showed a previous COVID-19 disease. After 7 days, the patient felt spasms or cramps in his left leg accompanied by a burning sensation from the neck to the middle of the spine when he tilted his head forward. 13 days after contacting COVID-19, he described numbness in his waist from umbilical part to the middle of the thigh. These symptoms were accompanied by perineum anaesthesia as well as urinary and faecal retention. The symptoms continued to progress; on April 5, numbness was felt from umbilical site

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Fig. 1. Thoracal MRI on April 8, 2021 (T2)

to the feet, and two days later the patient was admitted to the ER as described above.

The patient had no medical history of chronic diseases or spinal trauma. Neurological examination showed brisk reflexes in both legs, hypesthesia from Th8 and below, hyperalgesia in feet, urinary and faecal retention. Other systems appeared to be with no changes. Laboratory tests were performed, routine peripheral blood test and blood biochemistry were normal.

A lumbar puncture was performed and cerebrospinal fluid (CSF) sample was taken for analysis. The CSF was reddish with the addition of artificial blood. Microscopy revealed moderate pleocytosis consisting mainly of mononuclear cells (90%) and neutrophils (26 WBC/mL), and red blood cell (RBC) count of 1. CSF glucose concentration was 3.22 mmol/L (capillary blood glucose 5.6 mmol/L) and was considered normal while protein concentration was elevated (0.85 g/L). CSF lactates (1.55 mmol/L) and chlorides (127 mmol/L) were also assessed as normal. Anti-aquaporin-4 (anti-AQP-4) and anti-oligodendrocyte glycoprotein (Anti-MOG) and oligoclonal bands (OCBs) were not detected in CSF. To rule out an infectious cause, a scan of chronic infections in blood and CSF was performed. *Treponema pallidum* hemagglutination assay (TPHA) for neurosyphilis and human immunodeficiency virus (HIV) 1 and HIV 2 antigen p24 in blood came negative. Cytomegalovirus (CMV) IgG were 117.2 AU/mL and IgM were absent in blood. *Borrelia burgdorferi* (*B. Burgdorferi*) immunoglobulin (Ig) M and IgG in blood and CSF also showed negative re-

sults. PCR for SARS-CoV-2 from nasopharyngeal swab was tested several times and all of them confirmed negative result.

Radiological imaging tests were also carried out to clarify the diagnosis. On April 8, myelopathy signs in the magnetic resonance imaging (MRI) scans of thoracic site were absent (Fig. 1).

Brain MRI did not show any signs of demyelinating or other diseases. The patient was consulted by a neuro-ophthalmologist. Visual acuity, visual field area and fundoscopic examination showed no abnormal changes in both eyes.

Based on clinical examination, laboratory and imaging findings, and according to multidisciplinary consensus, the clinical diagnosis of *Myelitis acuta virosa* was made. It was considered that most of the data pointed towards acute viral myelitis caused by COVID-19.

According to the clinical diagnosis, treatment with a daily 500 mg methylprednisolone pulse therapy combined with 500 mL 0.9% NaCl intravenously for 7 days and rehabilitation was initiated. Meanwhile, the treatment seemed to be effective, and hypesthesia began to regress. However, the patient reported hypesthesia below Th12 and persistent partial urinary and faecal retention, but limb strength was better and was evaluated 5/5. After 11 days from arrival at the ER, the patient was discharged for further observation in ambulatory rehabilitation.

After 2 weeks of ambulatory rehabilitation, the symptoms began to progress. The patient started to experience trouble with walking, dysfunction of the pelvic organs, and progression of regional type hypesthesia. Because of these symptoms, a neurologist in ambulatory department prescribed oral glucocorticoids and baclofen. On June 15, MRI of Th8-S2 site was performed. The scan showed no myelopathy signs. Despite treatment, the symptoms continued to progress and imaging tests were repeated in dynamics. On August 23, MRI scans of thoracic and cervical sites revealed multiple poorly differentiated lesions of myelopathy without significant mass effect or contrast enhancement. These were considered changes after previous myelitis (Fig. 2 and Fig. 3).

Due to the worsening clinical features and negative MRI dynamics, the patient was re-hospitalized at the Neurology Department of the Hospital of Lithuanian University of Health Sciences Kaunas Clinics on August 26, 2021. Neurological examination showed normal (five out of five (5/5)) proximal and distal strength in both arms. In both legs proximal strength was 3/5 and distal strength was 1/5 bilateral. Muscular tone in legs was increased and showed spasticity. Legs reflexes were intensified on both sides with clonus and presentation of pathological Babinski reflexes bilateral. The patient had difficulties walking, he could not walk on his own since August 23. Hypesthesia from Th7-8 was of a regional type as well as hyperalgesia in feet. The patient had urge urinary incontinence. Other systems showed no changes.

Treatment was initiated with a daily 1 g methylprednisolone pulse therapy combined with 500 mL



Fig. 2. Thoracal MRI on August 23, 2021 (T2)

0.9% NaCl intravenously for 5 days, baclofen 10 mg orally 2 times a day, and azathioprine 25 mg orally once a day in conjunction with plasmapheresis. A significant positive effect of this therapy was noted. Strength in the legs was restored to 4/5, the patient could walk without walking aids,

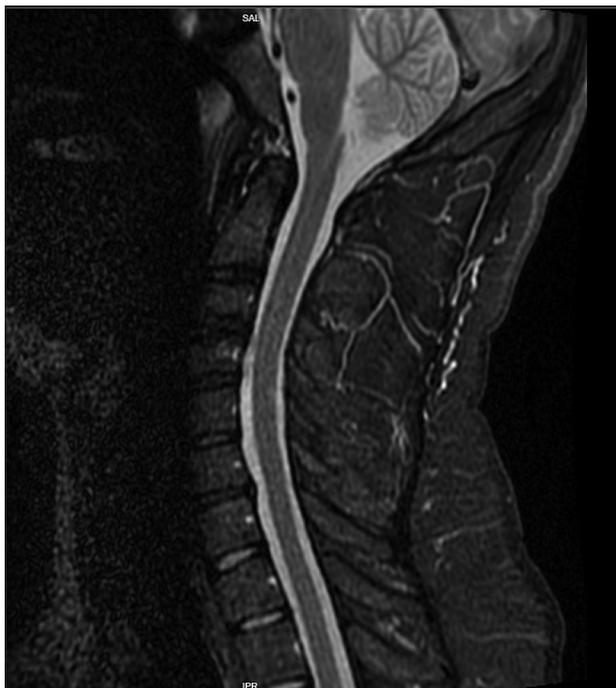


Fig. 4. Cervical MRI on March 17, 2022 (T2)



Fig. 3. Cervical MRI on August 31, 2021 (T2)

and there was also a decrease in leg spasticity. However, sensitivity derangement remained, but lower in dynamics. Unfortunately, impairment of pelvic organs persisted. On September 9, the patient was discharged for ambulatory rehabilitation after increasing the ambulatory dose of azathioprine to 100 mg per day.



Fig. 5. Thoracal MRI on March 17, 2022 (T2)

On March 17, control MRI scans of thoracic and cervical sites were performed. Scanning showed a decrease in most lesion size, and worse differentiation (Fig. 4 and Fig. 5). These signs are considered as slightly positive dynamics. Treatment with azathioprine 50 mg 2 times a day was continued.

DISCUSSION

Depending on the onset of the lesion, acute idiopathic inflammatory myelitis is divided into transverse myelitis (grey and white matter), poliomyelitis (grey matter), and leucomyelitis (white matter). The most well-known viruses that cause myelitis are adenoviruses, Coxsackie A and B, CMV, enteroviruses, Epstein-Barr virus (EBV), enteric cytopathic human orphan (ECHO) viruses, *Herpes simplex* and *Herpes zoster*, polioviruses, and sometimes HIV infection. Myelitis rarely occurs after vaccines, bacterial or parasitic infections [3].

Covid-19 pathogenesis involves direct virus damage, impairment caused by cytokine “storm”, and molecular mimicry leading to sensitization of the immune system. The exact mechanism is related to the time from the onset of the infection to neurological symptoms. Our patient developed neurological symptoms 7 days after infection, so it is believed that the cause of his symptoms is a direct virus damage and a cytokine “storm”. Later relapses can be explained by molecular mimicry between the virus and myelin, which causes sensitization of the immune system to neuron surface antigens [4–7]. According to the scientific data, post-COVID-19 transverse myelitis has now been described in many cases worldwide, so the etiology of the transverse myelitis may be extended in the future.

Transverse myelitis mostly affects thoracic segments of the spinal cord, less often cervical. The lesions are mostly symmetrical and most often in several segments but can also extend through multiple segments. Our patient had lesions in multiple segments, and based on systematic review data, the average number of damaged segments was 10 [8]. It can be said that acute viral myelitis caused by COVID-19 is more severe than usually described.

The onset of transverse myelitis usually occurs 1-21 days after acute and mostly viral infection [1]. According to a systematic review of 20 patients with COVID-19 disease leading to transverse myelitis, the onset of neurological symptoms was from 6 hours to 7 days after infection [4]. Our patient felt the first symptoms of limb spasms and cramps after 7 days and, despite progression, did not present to the ER until 12 days after the first symptoms, when they were severe.

The diagnosis of transverse myelitis can be difficult and involves wide differential diagnostics: multiple sclerosis, neuromyelitis *optica spectrum* disorders, Anti-MOG associated demyelisation, paraneoplastic syn-

dromes, vitamin B12, vitamin E, and copper deficiency, cerebrovascular causes, radiotherapy that affects spinal cord [1]. Based on these possible causes of the symptoms, the clinical diagnosis was reached in our case using differential diagnosis.

Cerebrospinal fluid test was also consistent with case series and systematic reviews. 30% of patients have moderate pleocytosis, Anti MOG, and Anti AQP4 are also negative. In addition, SARS-CoV-2 PCR was also absent in CSF, which made diagnostics even more complicated [3].

The first choice of imaging test should be MRI (myelography may be also considered). About 40% of cases show no changes or they are not specific. Usually, transverse myelitis lesions involve 3-4 segments [9], but in COVID-19 caused myelitis, multiple segments are more common as previously described, averaging 10 [8]. In our case, the lesions became visible 5 months after symptom onset and were hyperintense in T2.

Initially, the treatment consists of treating or correcting the etiological factor if it is identified. First-line therapy is pulse glucocorticoid therapy with methylprednisolone 1 g for 3-5 days. If clinical signs are significant, plasmapheresis should be considered. When disease relapses, the solution is individual but should include immunosuppressive therapy such as mycophenolate mofetil, azathioprine, or rituximab. Treatment of symptoms, including baclofen, oxybutynin, and gabapentin for hyperalgesia, is recommended in conjunction with early rehabilitation [1].

The prognosis of this disease depends on many factors. In most cases, transverse myelitis does not reoccur after one relapse, but if the patient has other systemic diseases, the probability of recurrence can reach more than 70%. If MRI do not show any changes the disease can also manifest as multiple sclerosis. One-third of patients recover without neurological deficit and another third may have significant residual disability. Recovery can last from 6 to 24 months [1].

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SKERSINIS MIELITAS PO COVID-19: KLINIKINIS ATVEJIS

Santrauka

Šiuo metu daugėja duomenų apie po COVID-19 pasireiškiančius neurologinius sutrikimus. Todėl manome, kad dėmesys jiems galėtų praplėsti visos neurologų bendruomenės supratimą apie šią ligą ir pasiruošti ateities pandemijoms. Ypač svarbu yra įvertinti ir atpažinti potencialias neurologines išraiškas bei komplikacijas, nulemtas COVID-19, nes kai kurios iš jų greitai progresuoja ir reikalauja skubaus gydymo.

Pristatome klinikinį skersinio mielito atvejį po COVID-19 35-erių metų amžiaus vyrui, kuris buvo gydytas LSMUL Kauno klinikų neurologijos klinikoje.

Raktažodžiai: skersinis mielitas, COVID-19.

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