Acute transverse Myelitis associated with Covid-19. Case Report.

Mielitis transversa aguda asociada a Covid-19. Reporte de caso.

Victoria Montero R.[1], Camilo Sepúlveda S.[1], Pamela Navarrete J.[1], Julio Vargas O.[2], David Sáez M.[3]

ABSTRACT

Since the beginning of the COVID-19 pandemic in 2019, numerous clinical manifestations of the disease caused by this virus have been described, highlighting respiratory, hematological, cardiovascular, and neurological compromise. Among the neurological manifestations and/or complications, there is acute transverse myelitis due to COVID-19(1), whose diagnosis has been made mainly clinical-imaging and PCR or serology (+) for COVID-19, with management and results not always lucky.

We present the case of a patient with longitudinally extensive acute transverse myelitis in relation to COVID-19, treated with clinical success with rituximab.

Keywords: *Myelitis, COVID-19, Rituximab.*

1. Neurology Resident, Faculty of Medicine South Campus - University of Chile. Barros Luco Trudeau Hospital.
2. Adjunct Professor, Faculty of Medicine South Campus - University of Chile. Neurologist Barros Luco Trudeau Hospital.
3. Associate Professor, Faculty of Medicine South Campus - University of Chile. Neurologist Barros Luco Trudeau Hospital.

Received: 10-17-2023
Approved: 01-26-2024

Authorship statement: Authors approved this submission.
Conflicts of interest: The authors declare that they have no conflicts of interest that could bias the content expressed in this article.
Funding: Self-funded article, did not receive funding from any project or agency.

CASE PRESENTATION

We present the case of a 51-year-old male patient, previously self sufficient, with a history of arterial hypertension, diabetes mellitus type(2) not requiring insulin, recurrent urinary infections, coronary heart disease and untreated auricular fibrillation. He had a history of using cocaine until one year prior to consultation. The first dose of the SARS CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) vaccine (Pfizer®) was received on March 20, 2021.

On March 30, 2022, his general state was compromised. He had a headache, odynophagia and myalgias. He consulted in primary care, where a SARS-CoV-2 antigen test was performed, which resulted positive and was treated symptomatically with an outpatient treatment. The symptoms subsided rapidly and the discomfort continued until three days later when he started with burning pain in the supraumbilical, anterior and posterior band. Two days later, he reported progressive weakness of both lower extremities, distal and proximal, which made it impossible to walk for three or four days. During this period, he also presented a compromised sphincter and sexual dysfunction. There was no sensitive involvement of the lower and upper extremities, nor did he present difficulty breathing. He finally consulted on April 17, at the Barros Luco Hospital Emergency Service, where the general physical examination highlighted the presence of a vesical globe, and the neurological examination showed a paraparesis M3 proximal - M1 distal, with decreased tone, present and symmetrical osteotendinous reflexes (ROT), with indifferently bilateral plantar cutaneous reflex (RCP) . A TAC (computed axial tomography) of the brain and dorsolumbar spine was performed and resulted in alterations. TAC of the chest showed a bilateral multifocal pneumopathy with characteristics of small airway disease. An Angio-TAC of aorta ruled out a dissection. The lumbar puncture (PL) showed a LCR (cerebrospinal fluid) with pleocytosis of 20 leukocytes/mm3, proteins 0.66 mg/dL, glucose 106 mg/dL; Gram stain with few leucocytes and bacteria culture negative, negative filmarray . He was hospitalized for studies, and a complete blood count, HSV (erythrocyte sedimentation rate), kidney function, plasma electrolytes, coagulation tests, liver profile, C-reactive protein, immunological profile, and vitamin B12 levels were performed, which were normal. Tumor markers, serology for HIV (acquired immunodeficiency virus), HTLV I – II (human T-lymphotropic virus 1 and 2) and non-reactive VDRL (venereal disease research laboratory) were also negative.

The patient rapidly progressed in three days to paraplegia and a suspended thermoalgesic level T5-T8. The study was amplified with IgG anti-AQP4 antibodies and serum anti-MOG antibodies, both were negative. A new PL showed a clear liquid, leucocytes 8/mm3, proteins 0.65 mg/dL, glucose 138 mg/dL, negative new film array, Gram stain with scant amount of leucocytes and no bacteria, new culture resulted negative. A study of oligoclonal bands (BOC) that resulted positive with pattern type (2) was requested. If a sample of peripheral blood and CSF is taken to perform a qualitative test of anti-SARS-CoV-2 antibodies, resulting in IgG (+) and IgM (-) both in blood and in CSF.

In the nuclear magnetic resonance (RNM) of the total spine, an extensive acute inflammatory myelopathy was highlighted, affecting cervical and dorsal segments **(Figure 1)**.

Given that he showed symptoms and images compatible with acute myelitis, pulses of intravenous methylprednisolone 500 mg/day were started for 5 consecutive days, with paraplegia, thermoalgesic level T5 and sphincter compromise persisting. There was no clinical progression towards the upper extremities or any degree of respiratory compromise. On April 30th, a treatment with plasmapheresis completing 5 cycles was started: there was improvement in strength and on May 12, M1-M2 of both distal LES was quantified. Finally, rituximab in two pulses was presribed. At discharge he had proximal M0 and distal M1-M2 paraparesis of both LES.

The patient continued with kinesiotherapy and was monitored, with progressive improvement in muscle strength observed. Three months after the onset of the symptoms, the patient achieved M3 Iliopsoas, M2-M3 quadriceps, M2 in tibialis anterior and gastrocnemius, without sensory level, but with persisting sphincter involvement. At eight months he was able to stand and at nine months he was able to walk independently with intermittent use of a cane. After ten months of evolution, the patient attended a check-up and had an

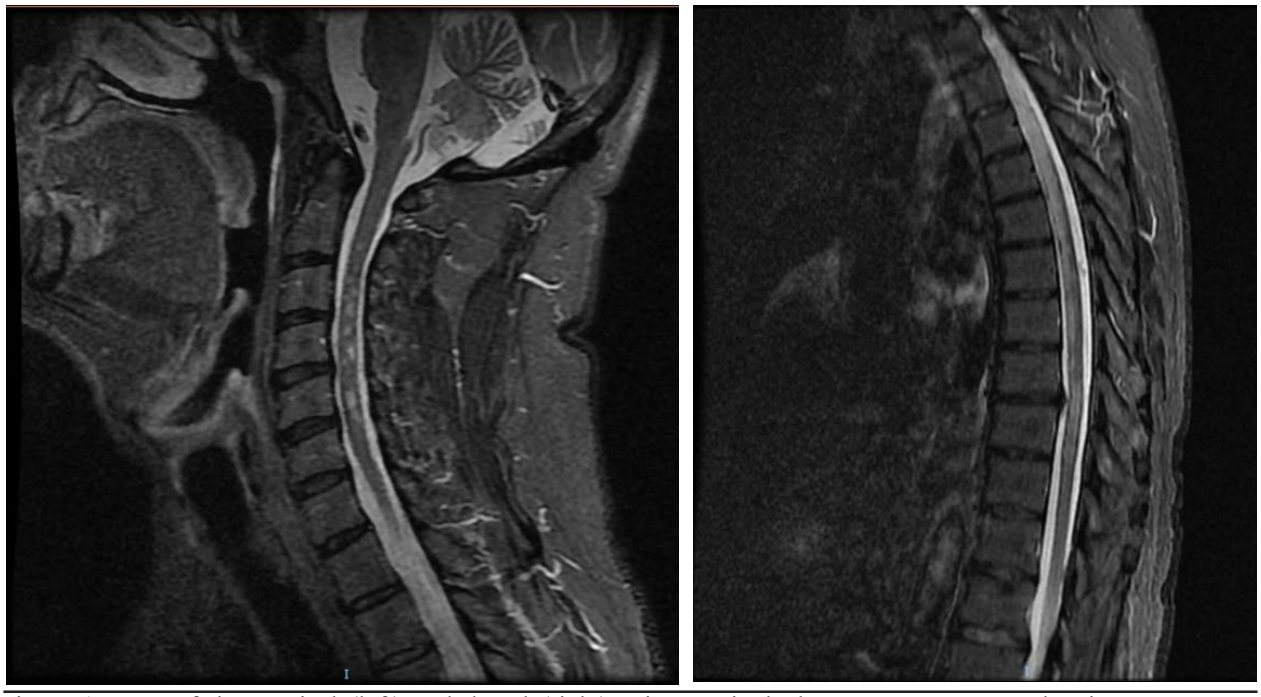

Figure 1. MRI of the cervical (left) and dorsal (right) spine, sagittal plane STIR sequence showing extensive segmental and continuous hyperintense lesions in the spinal cord.

independent gait, with M5 strength of 4 proximal and distal extremities, with muscle fatigue mainly of the iliopsoas, practically normal tone, ROT present and symmetrical, clonus in both lower extremities and Bilateral flexor CPR. There was no sensory alteration. He achieved control of the anal sphincter, but not the urinary sphincter, thus still requiring intermittent bladder catheterization. MRI of the total spine in February 2022 showed complete resolution of previously observed lesions, without any pathological findings **(Figure 2).**

Discussion

The patient received only the first dose of the vaccine against SARS-CoV-2 (Pfizer®). Ten days later he showed symptoms of COVID-19 and twelve days later, acute transverse myelitis (twentytwo days after vaccination). It is not possible to be sure if it is due to the adverse effect of the vaccine or an infection per se [2]

It should be mentioned that we did not have PCR SARS-CoV-2 in CSF, we stand out in this case from the diagnostic support of the presence of IgG and IgM of COVID-19 in peripheral blood and CSF, associated with the presence of BOC type 2 in LCR, which demonstrates the intrathecal synthesis of IgG possibly against SARS-CoV-2, consistent with the immunoinflammatory process of the CNS that occured in our patient. There have been reports and confirmation of the relationship between acute transverse myelitis and COVID-19 in other cases in literature. [3]

The treatment suggested in case reports, was corticoids and, in some cases, intravenous immunoglobulin G (IgG IV) and/or plasmapheresis [4,5,6,7, 8], with inconclusive results. The patient received treatment in our center, initially with intravenous methyprednisolone, then plasmapheresis and finally rituximab. There are reported cases where it is administered as the last drug in cases of ADEM associated with COVID-19[9,10]. Our patient had no brain lesions.

Even though, the patient had a poor initial response, the follow-up allowed to observe the long-term progressive improvement after treatment, suggesting rituximab therapy as an alternative in those patients who do not respond or who do so minimally to the initial treatment with corticoids in high doses. It does require more experience with a greater number of cases available in literature.

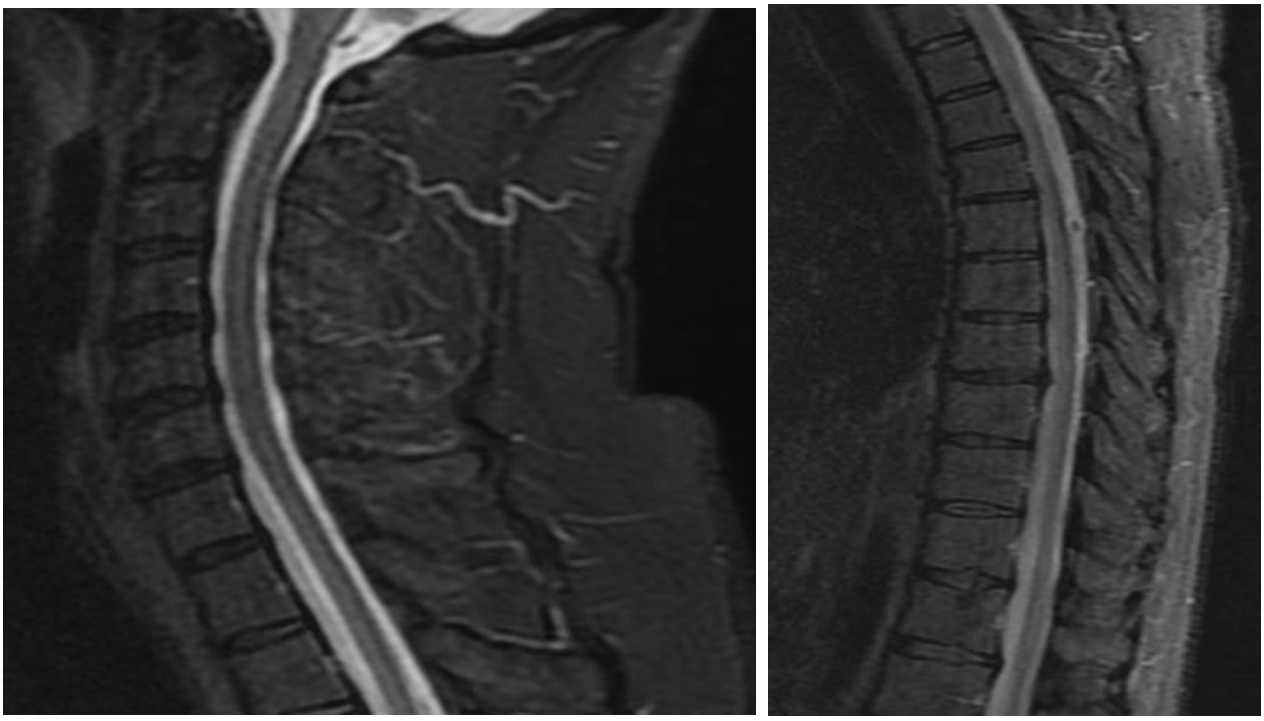

Figure 2. MRI cervical (left) and dorsal (right) spine sagittal plane STIR sequence taken in February 2022. No lesions.

On the other hand, it is not possible to rule out that it corresponds to an immune-mediated phenomenon related to the COVID19 (Pfizer®) vaccine. We cannot explain it completely; but from the way it was presented, it makes us think that the cause of his myelitis was the viral infection.

CONCLUSION

Currently, the association between acute transverse myelitis and COVID-19 is clear, either post or parainfectious, as well as an adverse effect of the vaccine. The diagnostic method continues to vary, depending on the resources of each center, including clinical-radiological, PCR nasopharyngeal and in LCR, as well as IgG-IgM serological and in LCR. More and more case reports and systematic reviews support the use of corticosteroids in high doses as initial treatment. We also suggest considering the use of Rituximab in poorly responsive patients.

BIBLIOGRAPHICAL REFERENCES

1. Ahmad I, Rathore FA. Neurological manifestations and complications of COVID-19: A literature review. J Clin Neurosci. 2020 Jul;77:8-12. doi: 10.1016/j.jocn.2020.05.017. Epub 2020 May 6. PMID: 32409215; PMCID: PMC7200361.
2. Li X, Raventós B, Roel E, Pistillo A, Martinez-Hernandez E, Delmestri A, Reyes C, Strauss V, Prieto-Alhambra D, Burn E, Duarte-Salles T. Association between covid-19 vaccination, SARS-CoV-2 infection, and risk of immune mediated neurological events: population based cohort and self-controlled case series analysis. BMJ. 2022 Mar 16;376:e068373. doi: 10.1136/bmj-2021-068373. PMID: 35296468; PMCID: PMC8924704.
3. Schulte EC, Hauer L, Kunz AB, Sellner J. Systematic review of cases of acute myelitis in individuals with COVID-19. Eur J Neurol. 2021 Oct;28(10):3230-3244. doi: 10.1111/ene.14952. Epub 2021 Jul 12. PMID: 34060708; PMCID: PMC8239542.
4. Roma´ n GC, Gracia F, Torres A, Palacios A, Gracia K and Harris D (2021) Acute Transverse Myelitis (ATM):Clinical Review of 43 Patients With COVID-19-Associated ATM and 3 Post-Vaccination ATM Serious Adverse Events With the ChAdOx1 nCoV-19 Vaccine (AZD1222). Front. Immunol. 12:653786. doi: 10.3389/fimmu.2021.653786
5. Khedr EM, Karim AA and Soliman RK (2020) Case Report: Acute Spinal Cord Myelopathy in Patients With COVID-19. Front. Neurol. 11:610648. doi: 10.3389/fneur.2020.610648
6. Valiuddin H, Skwirsk B, Paz-Arabo P. Acute transverse myelitis associated with SARS-CoV-2: A Case-Report. Brain Behav Immun Health. 2020 May;5:100091. doi: 10.1016/j.bbih.2020.100091. Epub 2020 Jun 6. Erratum in: Brain Behav Immun Health. 2021 Dec 23;19:100408. PMID: 32835294; PMCID: PMC7275168.
7. Águila-Gordo D, Manuel Flores-Barragán J, Ferragut-Lloret F, Portela-Gutierrez J, LaRosa-Salas B, Porras-Leal L, Carlos Villa Guzmán J. Acute myelitis and SARS-CoV-2 infection. A new etiology of myelitis? J Clin Neurosci. 2020 Oct;80:280-281. doi: 10.1016/j.jocn.2020.07.074. Epub 2020 Sep 30. PMID: 33099361; PMCID: PMC7525324.
8. Advani S, Hosseini SM-M, Zali A, et al. Transverse myelitis after SARS-CoV-2 infection: Report of two cases with COVID-19. Clin Case Rep. 2021; 9:e05196. doi:10.1002/ccr3.5196
9. Shahmirzaei S, Naser Moghadasi A. Association of COVID-19 and Acute Disseminated Encephalomyelitis (ADEM) in the absence of pulmonary involvement. Autoimmun Rev. 2021 Mar;20(3):102753. doi: 10.1016/j.autrev.2021.102753. Epub 2021 Jan 18. PMID: 33476819; PMCID: PMC7836812.
10. Zelada-Ríos L, Pacheco-Barrios K, Galecio-Castillo M, Yamunaqué-Chunga C, Álvarez-Toledo K, Otiniano-Sifuentes R. Acute disseminated encephalomyelitis and COVID-19: A systematic synthesis of worldwide cases. J Neuroimmunol. 2021 Oct 15;359:577674. doi: 10.1016/j.jneuroim.2021.577674. Epub 2021 Jul 27. PMID: 34371208; PMCID: PMC8313793.

Correspondence:
Dr. David Sáez Méndez
Neurology Service Barros Luco Care Complex.
Gran Avenida 3204, San Miguel.
Cell: +569 92993254
Email: davidlsaez@gmail.com