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Case Report

Abulia Major and Hypoactive Delirium in COVID-19 Reversed with Methylprednisolone Pulse Therapy

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ABSTRACT

Background: Sars-CoV-2 is a member of the genus Betacoronavirus like the two other coronaviruses *viz.* SARS-CoV (Severe Acute Respiratory Syndrome Coronavirus) and MERS-CoV (Middle East Respiratory Syndrome Coronavirus). The SARS-CoV-2 infection has been associated with neuropsychiatric manifestations in acute and chronic COVID-19 (long COVID-19 syndrome), resulting in social consequences and worsening people's quality of life.

Case description: This article is a scenario of two cases of neurological manifestations resulting from infection by SARS-CoV-2 that were reversed with methylprednisolone in a pulse therapy regimen. The first case presents a young patient with symptoms similar to those existing in patients with Alzheimer's and Parkinson's diseases, whose final and presumable diagnosis was Abulia major. The second case exemplifies an elderly person admitted to the hospital due to hypoactive delirium triggered by a urinary tract infection hypothesis. The final diagnosis was hypoactive delirium secondary to COVID-19, with urinary manifestations from SARS-CoV-2 kidney injury.

Conclusion: The purpose of this article is to warn about phenomena related to COVID-19, whose treatment can be performed with high doses of corticosteroids and with drugs that act positively on dopaminergic and serotonergic pathways. Patient exams and more information are available in the appendix of this article.

Keywords: Methylprednisolone pulse-therapy; COVID-19; Dementia; Inflammation

INTRODUCTION

COVID-19 is a new disease that causes systemic disease, with the lungs just one of the injured organs. Neuropsychiatric symptoms have been reported in both acute COVID-19 and chronic inflammation triggered by SARS-CoV-2 infection [1,2-5].

This article presents two case reports, whose neuropsychiatric phenomena may have a causal relationship with SARS-COV-2 infection, both treated with methylprednisolone with good evolution. The article's draft is guided by the CARE case report guidelines https://www.care-statement.org/writing-a-case-report.

CASE DESCRIPTION

Case 1

A 40 years old man, married, presented rapid and progressive dementia with signs and symptoms that resembles Alzheimer's and Parkinson's diseases, the patient lost the ability to find and perform common daily tasks progressively. He forgot the sequence of undressing to take a shower; he did not know how to use cutlery for his meals, having to be reminded by his wife how he should conduct tasks. Associated with this scenario, he had tremors of a Parkinsonian characteristic. For 2 months, neurologists and psychiatrists evaluated him and prescribed behavioural disorders drugs. Exams ordered by neurology are cranial computed tomography, cranial magnetic resonance with no significant changes, laboratory tests not worthy of note in appendix.

Approximately 15 days after the current symptoms the patient had been diagnosed with oligosymptomatic COVID-19, without hospitalization. His wife and children remained with negative serology even with flu-like symptoms during the same patient's symptomatic period.

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Called to evaluate the case that approximately 10 days of follow-up was performed and requested more laboratory assessments such as HIV serology, CMV viral load, EBV, and herpes virus and all exams were negative, except for IgG CMV being positive. Autoimmunity evidence is also negative obsevered in appendix.

During the follow-up period, the patient's wife had information about the proposed hypotheses, and material about post-COVID-19 neurological manifestations was given to her, even though COVID-19 is a new disease with a shortage of material and publications about neuropsychiatric symptoms. After checking the exams already requested and considering the patient's evolution observed for ten days, the followed diagnostic possibilities were made post-COVID-19 autoimmune encephalitis or neuropsychiatric manifestations caused by toxic kynurenine by products. Both have treatments based on high doses of corticosteroids [6-9].

Given the situation without improvement after 2 months, given the exams and after the introduction of these new hypotheses, we jointly opted to perform methylprednisolone pulse for 3 days with the possibility of performing immunoglobulin in case of refractoriness, that is, a decision that respected the wife's understanding of the subject.

The protocol and patient's evolution are described below:

1. In first day (D1) METHYLPREDNISOLONE 1000 mg, intravenous, was performed, *via* infusion pump in 60 minutes.

2. Ivermectin 6 mg, two tablets as prophylaxis against disseminated strongyloidiasis.

3. Promethazine 25 mg, oral tablets, to prevent agitation, in addition to its anti-inflammatory effect on the central nervous system.

4. Citalopram 40 mg as an adjunct to treatment considering Serotonin and Dopamine deficiency after Sars-CoV-2 infection.

5. L-Dopa/Benserazide 100/25 mg, two oral tablets.

6. Vital signs were assessed, and no significant changes were noted.

The patient was submitted to therapy with 1000 mg of methylprednisolone for two more days with its progressive decrease in the following regimen:

Oral prednisolone-80 mg for three days, 60 mg for three days, 20 mg for three days, and 10 mg for three days. After seven and fourteen days respectively, he took a dose of 10 mg of prednisolone.

The patient evolved after 8 hours of drug infusion with normalization of cognitive function in a surprising way. During the first three days, he presented periods of neurological fluctuation, usually associated with a physical or psychological stressor. The prescription of rest for 1 month was performed. The patient had a good evolution, with no return to dementia [10-12].

The phenomena presented by the patient resembled a mixture of Parkinson's Disease (PD) and Alzheimer's Disease (AD) [13-15], similar to rapid and progressive dementia. Having performed tests that could be requested and associated with the patient's clinical manifestations, the diagnosis was not closed, but there were two main possible hypotheses: a) anatomical: the central nervous system; syndromic: dementia-like manifestations of AD and PD; etiologic: a) possibly by toxic kynurenine by-products by IDO-1-mediated inflammation, depletion of dopaminergic and serotonergic pathways by ACE-2 internalization by SARS-CoV-2, or b) formation of autoantibodies, but with negative serology resulting from SARS-CoV-2 infection.

After 1 year of the manifestations and the resolution of the condition, the patient had a new infection by SARS-CoV-2 (with positive RT-PCR for SARS-CoV-2); however, milder than the first. A few days after the onset of symptoms, the patient began to experience tremors, anhedonia, and loss of self-confidence, requiring confirmation from the wife to perform any type of action or even to answer any questions that were asked. He also showed an attitude of muteness, was increasingly silent, and was not very reactive to situations. Initially, I called the patient by telephone, where he showed himself with spontaneous speech, reporting the changes he had realized in himself of unwillingness to perform daily activities, sadness, loss of self-confidence, and motor slowing. In a second moment, *via* video conference, the patient was silent, and for each question made by me, he needed confirmation from his wife. Unintentionally, this situation sets up "Miller Fisher's Telephone Effect" in appendix.

The possible diagnoses were, in the first COVID-19, Abulia major and, in the second Abulia minor. For this new situation, the use of prednisolone 1 mg/kg/day for 3 days, L-dopa, and citalopram triggered a global improvement in the patient. A joint discussion was performed with a psychiatrist who was performing the follow-up of the case (Table 1) [16].

Table 1: Timeline of the patient's (case 1) follow up.

Time line	Case observation
31-07-2022	COVID-19 Symptoms (The dates are hypothetical in order to preserve the patient's identity, but respect the chronology of the interventions).
14-08-2022	Dementia symptoms onset.
17-08-2022	Neurology's and psychiatrics assessment, mood disorder drugs, worsening of the symptoms.
22-10-2022	Infectious diseases specialist assessment and 10 days of follow up.
03-11-2022	Methylprednisolone pulse-therapy and good evolution after 12 hours of the corticosteroid infusion.
21-11-2023	Onset of the symptoms, but with less magnitude shown one year ago. Methylprednisolone 1 mg/kg/day and good evolution (Diagnose: Abulia minor, Encephalitis and Abulia major one year ago).

Case 2

A man of 93 years old, married, independent of performing daily activities, myelodysplasia as comorbidity [Katz=5 and Lawton=Partially dependent for 5 activities in appendix], is admitted to the emergency room due to acute hypoactive delirium. Here the infection screening was also performed. He had a chest X-ray without evidence of pneumonia, a blood count with mild anaemia associated with myelodysplasia, and leukocytes ~25,000 (slightly more than the patient usually presents in normal situations due to his comorbidity), and urine routine leukocyturia 70,000 haematuria 10,000, hyaline casts). The patient was initially diagnosed with delirium secondary to a urinary tract infection. However, when chest tomography was requested, it showed the tomographic pattern of acute COVID-19 in appendix. The patient began to present sluggishness 4 days ago, so it was assumed that the patient had been symptomatic for approximately 5 days, consistent with the chest tomography image presented in appendix.

According to epidemiology, signs, and symptoms, laboratory

changes, and tomographic imaging, COVID-19 was the main diagnosis. Urinary alterations are compatible with the lesions caused by SARS-CoV-2 in the renal parenchyma, which have often been confused with urinary tract infections [17,18]. The patient's daughter signed a consent form, and a pulse therapy regimen was performed with Methylprednisolone 250 mg once a day for three days [19-21]. The patient evolved to have an improved condition. He did not develop cytokine storm syndrome and was discharged on the fifth day of hospitalization.

RESULTS AND DISCUSSION

The two cases are in acute situations in patients who were previously healthy and independent or partially dependent to perform daily activities. We are facing a new virus with singularities that are still obstacles that prevent the realization of adequate therapy. It is essential to highlight that medical action must always be based on the ethics that govern the medical profession, on not harming, on offering comfort when there is no possibility of cure-always judging each situation properly and considering that the patient has a family that needs support.

The use of corticosteroids, although controversial, has gained increasing evidence in the treatment of COVID-19, with benefits when used on time and in high doses. Corticosteroids are historically used to treat viral or autoimmune meningoencephalitis and the cases presented are examples of good use of the drug, promoting patients' improvement of symptoms with a return to the health status they had before they became ill [7,8,22,23].

All the families involved signed a consent form for the data to be published; in addition, both families provided me with all the exams to help with the publication of the reported cases.

Methylprednisolone doses were based on the study published by Edalatfard et al. [24]. In addition, the higher doses between 500 mg and 1000 mg of Methylprednisolone were based on a pilot study that supported (observational results). The COVER-ME-UP study, based on the Tehran protocol. The COVER-ME-UP study was carried out after approval by the National Research Ethics Committee (Brazil) (CONEP: 39196620.2.0000.5463; Authorization number: 4.341.587) and after approval by the ethics committee of the Hospital where the study was carried out [26].

CONCLUSION

Corticosteroids have side effects, but they are medicines that have been used for many years, and in the face of an inflammatory disease due to SARS-COV-2 infection, the nonspecific target of steroids has been our best treatment. The purpose of this article is to warn about COVID-19-related phenomena, which can be treated with high doses of corticosteroids and drugs that act positively on dopaminergic and serotonergic pathways. The appendix of this article contains patient exams and additional information.

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I dedicate this work to all COVID-19 patients who have died or who remain with sequelae. To my colleagues in the emergency room of the university hospital of the University of Sao Paulo. To the patients' families that had the reported cases in this article.

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AUTHOR CONTRIBUTIONS

Luiz Zanella drafted this article and performed the follow-up of the patients.

CONFLICTS OF INTEREST

The author has no conflicts of interest.

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