Immunotherapy for recurrent orthostatic cerebral hypo-perfusion syndrome in recurrent COVID-19 infection

Hugues Ghislain Atakla MD1,6, Mahugnon Maurel Ulrich Déni Noudohounsi MD1,6, Fatoumata Lounceny Barry MD1,6, Carlos Othon Guelngar MD4,6, Fodé Abass Cissé MD5,6, Dismand Stephan Houinato MD6

1,6Neurology Department, University Hospital Center, Hubert Koutougou MAGA, Cotonou, Benin
1,6Laboratory of Non-communicable and Neurologic Diseases Epidemiology, Faculty of Health Science, University of Abomey-Calavi, Cotonou, Benin
2Monitoring and evaluation/WHO AFRO, Research Project Manager, Brazzaville, Congo
3Neurosurgery Department, University Hospital Center, Conakry, Guinea
4Neurology Department, Ignace Deen University Hospital Center, Conakry, Guinea

Date of submission: 9th March 2021 Date of acceptance: 5th May 2021 Date of publication: 1st June 2021

Abstract

Orthostatic hypotension, often interpreted as a fall in blood pressure as a person moves from lying or sitting to standing, has a direct impact on the brain. It results in a decrease in brain perfusion pressure and in many cases causes symptoms of transient cerebral hypoperfusion. This report treats a case of recurrent orthostatic hypotension in a field of recurrent COVID-19 infection, with a good clinical response to early immunotherapy. Signs of lung infection retroceded until complete disappearance under treatment with chloroquine sulfate and azithromycin. However, due to persistent signs of dysautonomy and paresthesias, the patient was subjected to intravenous immunoglobulin immunotherapy with good therapeutic response until the patient’s complete recovery 150 days after the start of treatment. The prognosis remains unknown at the time, as data is not yet available from large-scale studies on this subject.

Key words: Brain hypoperfusion, Immunotherapy, Recurrent, SARS-CoV-2.

Case Report

A 52-year-old woman with apyretic symptoms presented for a neurological consultation for leg pain, tingling paresthesia and burns in the lower and upper...
of dysautonomy, the patient has no sequelae of the disease. 150 days after the onset of the symptoms and leg pain regressed within 60 days after initiation of immunoglobulin at a dose of 2g/kg/month for two months which was reduced to a dose of 1g/kg/week. It should be noted that orthostatic vertigo, headache, paresthesia which was reduced to a dose of 1g/kg/week. It should be noted that orthostatic vertigo, headache, paresthesia was noted that orthostatic vertigo, headache, paresthesia was noted that orthostatic vertigo, headache, paresthesia was noted and the patient was put under observation for an etiological investigation. The cardiac assessment was normal and the search for other pathologies, particularly neurological and familial, with a degenerative appearance was not productive.

In addition, worsening of the patient’s condition was noticed with onset of cough, dyspnea and hypoxemia. The patient was transferred to the intensive care unit where she was given high-flow oxygen and non-invasive ventilation pending a positive SARS-CoV-2 reverse transcriptase PCR (RT-PCR) result. At this stage, the repeated bioassay revealed a biological inflammatory syndrome with a CRP of 38 mg/dl and lymphopenia. The D-dimer was 11644µg/L. Thoracic CT scan showed viral pneumonia (Figure 1).

Appropriate sanitary measures were taken and the patient was subjected to chloroquine sulfate in combination with azithromycin. After 10 days of treatment, the clinical respiratory signs totally regressed with more or less stationary persistence of dysautonomic signs and paresthesias. Following two repeated tests for SARS-CoV-2, which were negative; and the unsuccessful search for other causes of dysautonomic disorders, we suspected that an autoimmune mechanism was at the origin of the symptoms. The patient was treated with intravenous immunoglobulin at a dose of 2g/kg/month for two months which was reduced to a dose of 1g/kg/week. It should be noted that orthostatic vertigo, headache, paresthesia and leg pain regressed within 60 days after initiation of immunotherapy. 150 days after the onset of the symptoms of dysautonomy, the patient has no sequelae of the disease.

Discussion

This report describes a case of orthostatic hypotension syndrome in a patient with recurrent COVID-19 infection with a good response to immunotherapy. This case is the first observation in our country since the first case of SARS-CoV-2 infection recorded in our country. The onset of orthostatic hypotension was preceded by sensory disturbances such as paresthesia of the limbs. This peripheral nervous system dysfunction with dysautonomic disorders in the context of COVID-19 infection was also recently reported by Peter Novak.5 This disorder suggests an early damage of the peripheral nerve roots. In addition, we also noticed clinical signs of cerebral hypoperfusion, which led us to conclude that the CNS was simultaneously affected, even though we were not able to perform a transcranial Doppler scan in order to assess the speed of the blood flow. Nevertheless, there are several recent studies that support the thesis that the nervous system in general is affected by SARS-CoV-2 aggression.6-7

Whatever the cause, it is always a failure of the physiological mechanisms of blood pressure regulation involved in the transition to orthostatism.5 According to currently available data, orthostatic hypotension has rarely been associated with an infectious pathology of viral origin. However, several authors report cases of peripheral neuropathy or dysautonomia in the setting of SARS-CoV-2 infection or post COVID-19 infection.6,3,5,8 As a rule, orthostatic hypotension is related to drug intake, prolonged decubitus in the elderly subject, bulky varicose veins, hypovolemia,9,11 of which the etiological research in our case revealed none of these. Considering the history of our patient, other cases of dysautonomia of infectious origin reported in the literature, and the biological evidence that testifies the cytokine cascade following the viral aggression, we believe that an autoimmune reaction may have been triggered, secondary to the recurrence of the SARS-CoV-2 infection. We have therefore established

Figure 1: Bilateral diffuse frosted glass infiltrates
that the autoimmune reaction may have been the cause of the dysautonomia, thus affecting the vessels and/or baroreceptors in their roles of routing/serving the brain and systemic structures. Some recently described cases, such as peripheral neuropathies including Guillain-Barré polyradiculoneuritis (GBS)\(^1\) induced by SARS-CoV-2 infection, lead to the same conclusion. Moreover, the rapid therapeutic response to immunotherapy suggests the same mechanism as in GBS. Immunoglobulin at the dose described above resulted in complete resolution of symptoms by the 4th month of treatment. However, the subject deserves further reflection, by a large-scale investigation to better define it and establish a fixed therapeutic consensus.

**Conclusion**

In summary, this report describes an orthostatic cerebral hypo-perfusion and sensory neuropathy following an SARS-CoV-2 infection, adding to the large list of post-infection complications of COVID-19. The autoimmune reaction seems to be the mechanism involved and the conduct of good immunotherapy could facilitate the total regression of symptoms.

**Conflict of Interest:** None  
**Source(s) of support:** None

**References**

1. Asadi-Pooya AA, Simani L. Central nervous system manifestations of COVID-19: A systematic review. Journal of the Neurological Sciences. 2020;413:16832. https://doi.org/10.1016/j.jns.2020.116832
2. Montalvan V, Lee J, Bueso T, et al. Neurological manifestations of COVID-19 and other coronavirus infections: A systematic review. Clin Neurol Neurosurg. 2020;194:105921.
3. Eshak N, Abdelnabi M, Ball S. Dysautonomia: An overlooked neurological manifestation in a critically ill COVID-19 patient. Am J Med Sci. 2020;360(4):427-9. https://doi.org/10.1016/j.amjms.2020.07.022
4. Atakla HG, Condé K, Neishay A, et al. Cerebrovascular accidents indicative of COVID-19 infection: About 4 observations in Guinea: Accidents vasculaires cérébraux révélateurs d’infection au COVID-19: A propos de 4 observations en Guinée. Pan Africa Medical Journal. 2020, 35(2):65.https://doi.org/10.11604/pamj.supp.2020.35.2.23751
5. Novak P. Post COVID-19 syndrome associated with orthostatic cerebral hypoperfusion syndrome, small fiber neuropathy and benefit of immunotherapy: A case report. eNeurological Sci. 2020;21:100276. https://doi.org/10.1016/j.ensci.2020.100276
6. Montalvan V, Lee J, Bueso T, et al. Neurological manifestations of COVID-19 and other coronavirus infections: A systematic review. Clin Neurol Neurosurg. 2020;194:105921.
7. Kaufmann H, Nordlie-Kaufmann L, Palma JA. Baroreflex dysfunction. N Engl J Med. 2020;382(2):163–78.https://doi.org/10.1056/NEJMra1509723
8. Hugues Ghislain Atakla, et al. Acute Guillain-Barré polyradiculoneuritis indicative of COVID-19 infection: A case report. Pan African Medical Journal. 2020;35(2):150.https://doi.org/10.11604/pamj.supp.2020.35.150.25745
9. Danziger N, Alamowitch S. Neurologie l2e édition actualisée, 12th ed. Paris: Med-Line Editions;2018. ISBN 978-2-84678-232-6
10. Güler S, et al. Intracranial hypotension is a rare cause of orthostatic headache: A review of the etiology, treatment and prognosis of 13 cases. Journal of the Neurological Sciences. 2013;333:e481–e518.https://doi.org/10.1016/j.jns.2013.07.1706
11. Raffoul J, et al. A rare cause of recurrent orthostatic hypotension refractory to conventional treatment. American college of cardiology. JACC. 2016;67(13). https://doi.org/10.1016/S0735-1097(16)31251-7
12. Dalakas MC. Guillain-Barré syndrome: the first documented COVID-19-triggered autoimmune neurologic disease: more to come with myositis in the offing. Neurology, Neuroimmunology & Neuroinflammation. American Academy of Neurology. 2020;5: e781.https://doi.org/10.1212/NXI.0000000000000781