References

1. Li Y, Li M, Whang M, et al. Acute cerebrovascular disease following COVID-19: a single center, retrospective, observational study [published online ahead of print, 2020 Jul 2]. Stroke Vasc Neurol. 2020;svn-2020-000431. 2020, http://dx.doi.org/10.1136/svn-2020-000431.
2. Oxley TJ, Mocco J, Majidi S, et al. Large-vessel stroke as a presenting feature of covid-19 in the young. N Engl J Med. 2020;382:e60, http://dx.doi.org/10.1056/NEJMc2009787.
3. Hasan A, Paray BA, Hussain A, et al. A review on the cleavage priming of the spike protein on coronavirus by angiotensin-converting enzyme-2 and furin [published online ahead of print, 2020 Apr 22]. J Biomol Struct Dyn. 2020:1—9, http://dx.doi.org/10.1080/07391102.2020.1754293.
4. Mogi M, Horiuchi M. Effect of angiotensin II type 2 receptor on stroke, cognitive impairment and neurodegenerative diseases. Geriatr Gerontol Int. 2013;13:13—8, http://dx.doi.org/10.1111/j.1447-0594.2012.0.x0090.
5. Magro C, Mulvey JJ, Berlin D, et al. Complement associated microvascular injury and thrombosis in the pathogenesis of severe COVID-19 infection: a report of five cases [published online ahead of print, 2020 Apr 15]. Transl Res. 2020, http://dx.doi.org/10.1016/j.trsl.2020.04.007. S1931-5244(20)30070-0.
6. Conklin J, Frosch MP, Mukerji S, et al. Cerebral Microvascular Injury in Severe COVID-19. Preprint medRxiv. 2020; 2020.07.21.20159376. Published 2020 Jul 24. doi:10.1101/2020.07.21.20159376.

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Convulsive status epilepticus as a possible symptom of COVID-19 in a patient with intellectual disability and autistic spectrum disorder

Estatus epiléptico convulsivo como posible síntoma de infección por COVID-19 en un paciente con discapacidad intelectual y trastorno del espectro autista

Dear Editor:

Between 6% and 34% of patients with COVID-19 present neurological symptoms, with headache and myalgia being the most frequent.[1] Seizures, on the other hand, are less common.[2] The neurotropic nature of SARS-CoV-2 is yet to be confirmed, although the virus is thought to reach the central nervous system either through the haematogenous pathway[3] or through a transneuronal pathway via the olfactory nerve.[4]

We present the case of a 37-year-old man with history of bilateral ulnar neuropathy and recurrent pneumonia. He also presented moderate intellectual disability, an autistic spectrum disorder, and impulse control disorder. He was institutionalised in a long-stay psychiatry unit specialising in neurodevelopmental disorders and was under treatment with levomepromazine (250 mg/day), haloperidol (15 mg/day), olanzapine (30 mg/day), quetiapine (1000 mg/day), and clomipramine (300 mg/day). He developed fever associated with cough and dyspnoea; a PCR study for SARS-CoV-2 returned positive results. A chest radiography revealed infiltrate in the bases of both lungs (Fig. 1). Blood analysis revealed slight leukopaenia (3500 cells/mm^3), moderately elevated infection markers (C-reactive protein: 45.6 mg/L; ferritin: 9186.7 μg/L), and hypertransaminasaemia (ALT: 2692 IU/L; AST: 3160 IU/L; GGT: 127 IU/L), with no evidence of infection by hepatotropic viruses. Arterial blood gas analysis showed a pH of 7.49, with pO_2 of 68.5 mm Hg and pCO_2 of 32.4 mm Hg. With a working diagnosis of bilateral pneumonia and hepatitis secondary to SARS-CoV-2 infection, we started treatment with hydroxychloroquine (400 mg/12 h for 5 days), azithromycin

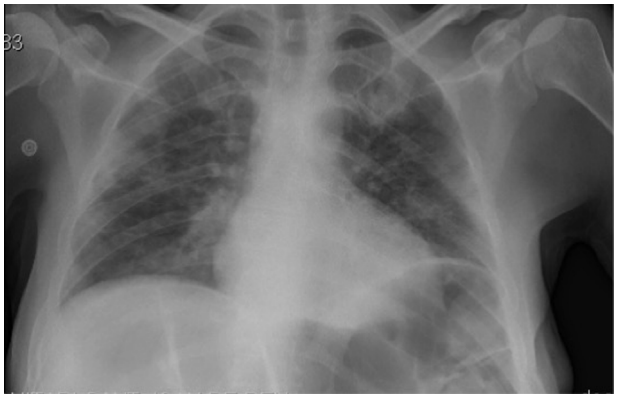

Figure 1 Chest radiography showing bilateral pulmonary infiltrate.

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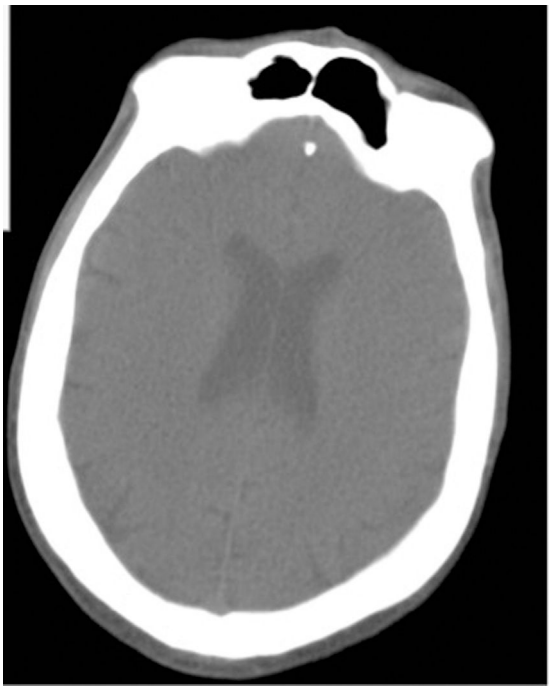

Figure 2 Head CT scan showing no alterations.

(500 mg/day for 5 days), methylprednisolone (250 mg/day for 3 days), and bemiparin sodium (7500 IU/day for 30 days). Twelve days after admission to the internal medicine department, the patient was discharged to the long-stay psychiatry unit, showing significant improvements in clinical (resolution of fever and respiratory symptoms) and laboratory parameters (C-reactive protein: 18 mg/L; ferritin: 641.6 μg/L; ALT: 100 IU/L; AST: 50 IU/L; GGT: 117 IU/L). Two days later, he presented an episode of status epilepticus, presenting as a single, uninterrupted, generalised tonic-clonic seizure of 15 minutes' duration, which resolved with 4 mg intravenous clonazepam. Neurological examination revealed stupor, absence of fever, a bite wound on the side of the tongue, conjugate gaze deviation to the left, and no meningism or paresis. An electrocardiography study showed sinus rhythm at 96 bpm, with no alterations of repolarisation; QTc was 0.459. Head CT findings were normal (Fig. 2). Blood analysis showed mild leukocytosis (14 500 cells/mm^3) and a C-reactive protein level of 31.8 mg/L. Electroencephalography and lumbar puncture were not performed due to clinical improvement and the risk of transmission of the SARS-CoV-2 virus. Two days later, the patient presented a second episode, manifesting as an atonic seizure of 3 minutes' duration. Following this seizure, we started treatment with valproic acid (1500 mg/day) and lacosamide (200 mg/day). Four weeks later, the patient remains seizure-free and has presented a marked improvement in aggressive and impulsive behaviour.

Discussion

This is the first reported case of tonic-clonic status epilepticus in a patient with SARS-CoV-2 infection and no previous history of epilepsy. The patient was receiving treatment with psychoactive drugs, which may have lowered the seizure threshold[5]; however, he had never previously presented seizures, and his treatment schedule had not been altered in the previous 3 months. At the time of the status epilepticus, fever had resolved and respiratory symptoms and levels of infection markers had improved considerably. A head CT scan revealed no abnormalities. While PCR testing of cerebrospinal fluid for SARS-CoV-2 was not performed, we believe that the virus may have played a role in the onset of status epilepticus. Research is ongoing into the neurotropic potential of SARS-CoV-2,[4,6] and only one manuscript published to date reports focal status epilepticus, in a patient with symptomatic epilepsy and SARS-CoV-2 infection.[7] Some studies report positive PCR results for SARS-CoV-2 in the cerebrospinal fluid in patients with encephalitis.[8] We considered it important to report this case, given the increased risk of seizures in patients with intellectual disability[9] or receiving antipsychotic drugs.[5]

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References

1. Ezpeleta D, García Azorin D. Manual COVID 19 para el neurólogo general. In: Ediciones SEN. Sociedad Española de Neurología; 2020. Available from: http://www.sen.es/attachments/article/2677/Manual_neuroCOVID-19_SEN.pdf
2. Lu L, Xiong W, Liu D, Liu J, Yang D, Li N, et al. New-onset acute symptomatic seizure and risk factors in Corona Virus Disease 2019: A Retrospective Multicenter Study. Epilepsia. 2020:1—5, http://dx.doi.org/10.1111/epi.16524.
3. Baig AM. Neurological manifestations in COVID-19 caused by SARS-CoV-2. CNS Neurosci Ther. 2020;26:499—501, http://dx.doi.org/10.1111/cns.13372.
4. Steardo L, Steardo L, Zorec R, Verkhratsky A. Neuroinfection may potentially contribute to pathophysiology and clinical manifestations of COVID-19. Acta Physiol (Oxf). 2020:e13473, http://dx.doi.org/10.1111/apha.13473.
5. Wu CS, Wang SC, Yeh IJ, Liu SK. Comparative risk of seizure with use of first- And Second-Generation antipsychotics in patients with Schizophrenia and mood disorders. J Clin Psychiatry. 2016;77:e573—9, http://dx.doi.org/10.4088/JCP.15m09898.
6. Li Z, Liu T, Yang N, Han D, Mi X, Li Y, et al. Neurological manifestations of patients with COVID-19: Potential routes of SARS-CoV-2 neuroinvasion from the periphery to the brain. Front Med. 2020:1—9, http://dx.doi.org/10.1007/s11684-020-0786-5.
7. Vollono C, Rollo E, Romozzi M, Frisullo G, Servidei S, Borghetti A, et al. Focal status epilepticus as unique clinical feature of COVID-19: A case report. Seizure. 2020;78:109—12, http://dx.doi.org/10.1016/j.seizure.2020.04.009.
8. Zhou L, Zhang M, Wang J, Gao J. Sars-Cov-2: Underestimated damage to nervous system. Travel Med Infect Dis. 2020:101642, http://dx.doi.org/10.1016/j.tmaid.2020.101642.
9. Robertson J, Hatton C, Emerson E, Baines S. Prevalence of epilepsy among people with intellectual disabilities: A systematic review. Seizure. 2015;29:46—62, http://dx.doi.org/10.1016/j.seizure.2015.03.016.

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Therapeutic approaches to multiple sclerosis in Central America and the Caribbean during the COVID-19 pandemic☆

Actitudes terapéuticas hacia la esclerosis múltiple en Centroamérica y el Caribe frente a la pandemia de SARS-CoV-2

Dear Editor:

The prevalence of multiple sclerosis (MS) in Central America and the Caribbean is low,[1] but its socioeconomic impact for healthcare systems is severe, considering the level of economic growth in these countries. Despite this limitation, most social security systems and some public healthcare systems in the region have dedicated a significant percentage of their budgets in recent years to the purchase of the varied and costly therapies approved by international agencies for the management of MS.[2] This situation has gradually emerged as an institutional response to public demand, supported by the need to provide a modern, appropriate neurological care to patients with MS.

The first cases of SARS-CoV-2 infection (and the first death in the region) were reported in Panama during the first week of March 2020. The pandemic had already reached critical incidence and mortality figures and had an unprecedented social impact in Europe, and particularly in Italy, Spain, France, and the United Kingdom. Cases in Central America were initially attributed to travellers reaching Panama from affected areas. Panama is an important hub of international connections as well as a final destination for business travel and tourism. In only 4 to 6 weeks, SARS-CoV-2 began to show community transmission, and rapidly affected all Central American countries and Caribbean islands, and especially Panama, Honduras, and the Dominican Republic.[3]

Addressing the theoretical possibility that patients with MS may be especially vulnerable to SARS-CoV-2 infection, due to neurological disability and the use of treatments affecting the immune system (in fact, several drugs cause persistent lymphocyte depletion), the Central American and Caribbean Forum on Multiple Sclerosis (FOCEM) has explored therapeutic approaches in this region during the pandemic. FOCEM is a neurological association of professionals from 10 countries, which was founded and officially registered to promote education, dissemination, research, and counselling for patients' groups in the region. We distributed a questionnaire specifically designed to analyse therapeutic approaches and decision-making among 93 identified professionals in the region. We used the online SurveyMonkey® system for data collection. The questionnaire included 30 questions inquiring about relapses reported from February 2020, the use of steroids or other drugs to treat these, and whether the patient in question was infected with SARS-CoV-2. We also enquired about the management of patients without the infection and those diagnosed with SARS-CoV-2, whether clinically or by laboratory testing. In line with international research,[4,5] the questionnaire classified therapies according to the theoretical risk of vulnerability to community transmission. Treatments classified as presenting very low risk included interferons, glatiramer acetate, and teriflunomide. Anti-CD20 monoclonal antibodies were classified as low risk; fumarates and natalizumab as medium risk; fingolimod as medium to high risk; and cladribine, alemtuzumab, mitoxantrone, and stem cell transplantation as high risk. Finally, the participants reported on the therapeutic approach they followed (or would theoretically follow) in the context of a relapse in patients with or without the infection, considering the risk associated with the treatment the patient is receiving. The questionnaire was available for 24 h. Mean completion time was 4 min and 30 s. Other aspects analysed included whether the treatment was conditioned by local situations (access to treatment, infusion, etc) and individualised decisions for each case.

Although the results are still being analysed,[6] a preliminary sample of data from participants from 9 countries (Guatemala, El Salvador, Honduras, Nicaragua, Costa Rica, Panama, Cuba, Dominican Republic, and Aruba) suggests that the great majority of professionals are working in social security systems, with half simultaneously working in the

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