



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Acknowledgement

The authors would like to give a special thanks to the colleagues and nurses at the departments of Neurology and Anesthesiology/reanimation and to Dr Mounir Zoubi.

REFERENCES

- [1] Zhao H, Shen D, Zhou H, Liu J, Chen S. Guillain-Barré syndrome associated with SARS-CoV-2 infection: causality or coincidence? *Lancet Neurol* 2020. [http://dx.doi.org/10.1016/S1474-4422\(20\)30109-5](http://dx.doi.org/10.1016/S1474-4422(20)30109-5). pii:S1474-4422(20)30109-5 [Epub ahead of print].
- [2] Camdessanche JP, Morel J, Pozzetto B, Paul S, Tholance Y, Botelho-Nevers E. COVID-19 may induce Guillain-Barré syndrome. *Rev Neurol* 2020. <http://dx.doi.org/10.1016/j.neurol.2020.04.003> [Epub ahead of print].
- [3] Sedaghat Z, Karimi N. Guillain Barre syndrome associated with COVID-19 infection: A case report. *J Clin Neurosci* 2020. <http://dx.doi.org/10.1016/j.jocn.2020.04.062> [Epub ahead of print].
- [4] Toscano G, Palmerini F, Ravaglia S, Ruiz L, Invernizzi P, Cuzzoni MG, et al. Guillain-Barré syndrome associated with SARS-CoV-2. *N Engl J Med* 2020. <http://dx.doi.org/10.1056/NEJMc2009191> [Epub ahead of print].

H. El Otmani^{a,f,*}
 B. El Moutawakil^{a,f}
 M.-A. Rafai^{a,f}
 N. El Benna^{b,f}
 C. El Kettani^{c,f}
 M. Soussi^{d,f}
 N. El Mdaghri^{d,f}
 H. Barrou^{e,f}
 H. Afif^{e,f}

^aDepartment of Neurology, Casablanca, Morocco

^bDepartment of Radiology, Casablanca, Morocco

^cDepartment of Anesthesiology and Reanimation, Casablanca, Morocco

^dDepartment of Biology, Casablanca, Morocco

^eDepartment of Pneumology, Ibn Rochd University Hospital, Casablanca, Morocco

^fMedicine and Pharmacy Faculty - Hassan II University, 1, Rue des Hôpitaux, Casablanca 90000, Morocco

*Correspondance: 67, rue Abou Allaa Zahr, N°20, Casablanca, Morocco.

E-mail address: hichamotmani@hotmail.com (H. El Otmani)

Received 18 April 2020

Accepted 20 April 2020

Available online 24 April 2020

<https://doi.org/10.1016/j.neurol.2020.04.007>

0035-3787/© 2020 Elsevier Masson SAS. All rights reserved.

Acute meningoencephalitis in a patient with COVID-19



A 69-year-old man with a 7-day history of fever and cough, was admitted to the University Hospital of Guadeloupe (French Indies) for confusion and severe headache. He had no medical history and reported having traveled to the Middle-East (cruise ship) with his wife 15 days before hospitalization. He did not report insect bites. A week after returning home, he presented fever, myalgia, cough, anosmia, ageusia, cervical pain, stiff neck, and diarrhea. At admission, he reported a worsening of his condition for 24 hours with painful and stiff neck and headache, confusion, walking disability with falls, and dyspnea. Noteworthy, his wife had also had isolated cough and ageusia for the past 10 days.

On examination, the patient was febrile (38.5 °C) with diffuse headache, neck stiffness, altered consciousness (Glasgow Coma Scale 14), confusion, swallowing disorders, and right-sided hemiparesis. Respiratory rate was increased (36/min), pulse rate was 95/min, blood pressure 160/89 mmHg, and oxygen saturation was 91% in ambient air.

Laboratory analyses showed increased C-reactive protein at 95 mg/L and creatine kinase level (655 U/L), raised transaminases (aspartate aminotransferase = 85 U/L, alanine aminotransferase = 94 U/L) and lactate dehydrogenase (442 U/L). Arterial partial pressure of oxygen was decreased at 64 mmHg with normal arterial partial pressure of carbon dioxide and pH. Chest computed tomographic scan was highly suggestive of COVID-19 (Fig. 1). Cerebrospinal fluid was purely lymphocytic ($37 \times 10^6/L$) with no red blood cells, an increased protein level at 84 mg/dL and normal glucose level. Brain MRI with gadolinium was normal. Electroencephalogram showed a bilateral slowed activity without seizures. The detection of SARS-CoV-2 by specific real-time reverse PCR (RT-PCR) was negative in nasopharyngeal swab and cerebrospinal fluid (CSF) on days 2 and 4 after admission but was positive in bronchoalveolar lavage on day 5. Using a similar biological tool, the search for *Influenza* virus was negative. RT-PCR for varicella-zoster virus, herpes simplex virus (HSV), and enterovirus in CSF were all negative. Other tests for endemic infections in our area were performed, but all negative.

The patient received nasal oxygen therapy. Acyclovir infusions were performed for 3 days and stopped when RT-PCR for HSV was found negative. We started hydroxychloroquine sulfate 200 mg, three times per day, and azithromycin 250 mg daily for 7 days. On hospital day 4, his neurological condition improved with normal consciousness and abatement of swallowing disorders. At discharged on day 10, mild neuropsychiatric features were still present with an alteration of executive functions. Montreal Cognitive Assessment was decreased to 26/30.

We describe meningoencephalitis one week after the onset of COVID-19 based on the combination of altered mental consciousness, fever, focal neurological defects, and cerebrospinal fluid abnormalities. We suspect the meningoencephalitis was related to COVID-19, possibly through a direct infectious mechanism although the virus was not detected in CSF [1].

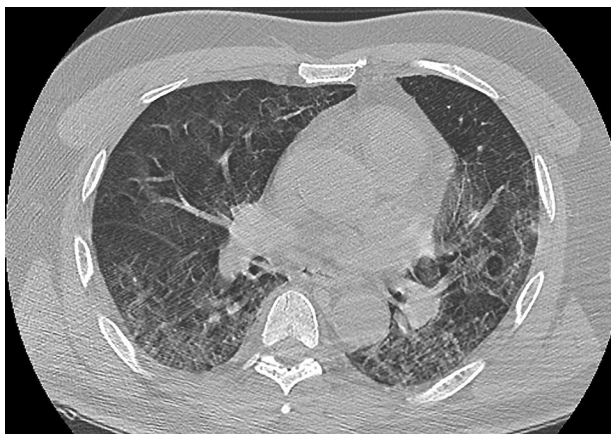


Fig. 1 – Chest CT scan in a patient with COVID-19 pneumonia and meningoencephalitis. Transverse thin-section CT scan on day 7 after symptom onset revealed bilateral, peripheral ground-glass opacities associated with crazy-paving pattern and subpleural lesions, predominant in the middle and lower lobes. There were no airway abnormalities, neither mediastinal lymphadenopathy nor pleural effusion. It is a typical image of a severe form (50% lung damage) of COVID-19 pneumonitis.

Detection of SARS-CoV-2 by RT-PCR in bronchoalveolar lavage at the time of lumbar puncture is rather in favor of a direct infectious than a post-infectious mechanism. Currently, we have no information about the sensitivity of specific RT-PCR in CSF nor the kinetics of the virus in the central nervous system. Manifestations such as impaired consciousness, acute cerebrovascular disease, seizure, diffuse cortical tract signs, dysexecutive syndrome have been reported among COVID-19 patients [2,3]. In addition, recent case reports described one patient with an acute haemorrhagic encephalopathy [4] and one patient with a meningoencephalitis associated with a COVID-19 infection [5]. Our observation provides further evidence suggesting that SARS-CoV-2 may be responsible for central nervous system damage, including meningoencephalitis.

Funding

Study funded by the French network for REsearch and ACTion targeting emerging infectious diseases (REACTing) of the French National Institute of Health and Medical Research (INSERM).

Consent for publication

Patient's consent has been obtained.

Disclosure of interest

Dr Chaumont reports having received travel grant from PEPS development, Roche and Pfizer. Dr Roze reports served on

scientific advisory boards for Orkyn, Aguettant, Merz-Pharma; received honoraria for speeches from Orkyn, Aguettant, Merz-Pharma, Medday-Pharma, Everpharma, International Parkinson and Movement disorders Society; received research support from Merz-Pharma, Orkyn, Aguettant, Elivie, Ipsen, Everpharma, Fondation Desmarest, AMADYS, Fonds de Dotation Brou de Laurière, Agence Nationale de la Recherche; received travel grant from Vitalair, PEPS development, Aguettant, Merz-Pharma, Ipsen, Merck, Orkyn, Elivie, Adelia Medical, Dystonia Medical Research Foundation, International Parkinson and Movement disorders Society, European Academy of Neurology, International Association of Parkinsonism and Related Disorders. Dr Couratier reports having received travel grant from Allergan, Novartis, Esai, UCB, Medtronic, Merck Serono, Biogen, LFB, Teva, Icomed, GSK, Genzyme, Aguettant, Cyberonics and Merz-Pharma. Dr Lannuzel reports having received research support from France Parkinson, PSP France, Agence Nationale de la Recherche, Fonds Européen de Développement Régional, French Ministry of Health, University Hospital of Guadeloupe, received honoraria for a speech from Association des Neurologues du Québec; received travel grant from Vitalair, PEPS development, Merz-Pharma, International Parkinson and Movement disorders Society. Dr Etienne and Dr Roger reports no disclosures.

REFERENCES

- [1] Steardo L, Steardo L, Zorec R, Verkhatsky A. Neuroinfection may contribute to pathophysiology and clinical manifestations of COVID-19. *Acta Physiol* 2020;e13473. <http://dx.doi.org/10.1111/apha.13473>.
- [2] Mao L, Jin H, Wang M, Hu Y, Chen S, He Q, et al. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. *JAMA Neurol* 2020. <http://dx.doi.org/10.1001/jamaneurol.2020.1127>.
- [3] Helms J, Kremer S, Merdji H, Clere-Jehl R, Schenck M, Kummerlen C, et al. Neurologic features in severe SARS-CoV-2 infection. *N Engl J Med* 2020. <http://dx.doi.org/10.1056/NEJMc2008597> [NEJMc2008597].
- [4] Poyiadji N, Shahin G, Noujaim D, Stone M, Patel S, Griffith B. COVID-19-associated Acute hemorrhagic necrotizing encephalopathy: CT and MRI Features. *Radiology* 2020. <http://dx.doi.org/10.1148/radiol.2020201187> [201187].
- [5] Moriguchi T, Harii N, Goto J, Harada D, Sugawara H, Takamino J, et al. A first case of meningitis/encephalitis associated with SARS-Coronavirus-2. *Int J Infect Dis* 2020. <http://dx.doi.org/10.1016/j.ijid.2020.03.062> [S1201971220301958].

H. Chaumont^{a,b,c,*}
 P. Etienne^d
 E. Roze^{c,e}
 C. Couratier^a
 P.-M. Roger^f
 A. Lannuzel^{a,b,c,g}

^aCentre Hospitalier Universitaire de la Guadeloupe, Service de Neurologie, Pointe-à-Pitre/Abymes, France

^bFaculté de Médecine de l'université des Antilles, Pointe-à-Pitre, France

^cFaculté de Médecine de Sorbonne Université, Institut National de la Santé et de la Recherche Médicale, U 1127, CNRS, Unité Mixte de Recherche (UMR) 7225, Institut du Cerveau et de la Moelle épinière, ICM, Paris, France

^dCentre Hospitalier Universitaire de la Guadeloupe, Unité d'Hospitalisation de Courte Durée, Pointe-à-Pitre/Abymes, France
^eAP-HP, Hôpital de la Pitié-Salpêtrière, Département de Neurologie, Paris, France

^fCentre Hospitalier Universitaire de la Guadeloupe, Service d'Infectiologie, Pointe-à-Pitre/Abymes, France

^gCentre d'investigation Clinique Antilles Guyane, Inserm CIC 1424, Pointe-à-Pitre, France

*Corresponding author at: Department of Neurology, University Hospital of Guadeloupe, 97139 Pointe-à-Pitre/Abymes, French West Indies, France.

E-mail address: hugo.chaumont@chu-guadeloupe.fr (H. Chaumont)

Received 24 April 2020

Received in revised form 29 April 2020

Accepted 29 April 2020

Available online 11 May 2020

<https://doi.org/10.1016/j.neurol.2020.04.014>

0035-3787/© 2020 Elsevier Masson SAS. All rights reserved.

First case of Covid-19 presented with cerebral venous thrombosis: A rare and dreaded case



1. Background

The corona virus disease 2019 (COVID-19) is a newly recognized infection which is pandemic [1]. Patients with COVID-19 commonly have neurological manifestations [2]. COVID-19

presents with a variety of phenotypes range from asymptomatic to severe, rapid multiorgan dysfunction and death. The mechanisms are multifactorial but may include a hypercoagulable state with micro- and macro-circulatory thrombosis. The virus can bind to endothelial cells, damage the vessels and lead to platelet aggregation. The coagulation function is deranged [3]. Clots in the small vessels of all organs were described [4]. In this study we report an unusual presentation of COVID-19 with cerebral venous thrombosis (CVT).

2. Case report

A 65-year-old previously healthy male was admitted to the emergency department in ALzahra hospital, Isfahan, Iran with complaint of loss of consciousness, upward gaze and tongue biting. Upon arrival, he was drowsy. He had no focal neurological sign. Vital signs were remarkable for oxygen saturation of 90% on room air but otherwise stable. He didn't have any complain of respiratory symptom. Blood investigation showed an increased white cell count with 6% lymphocytes, normal CRP and ESR but increased CPK and LDH. Brain imaging demonstrated hemorrhagic infarct in right temporal and right sigmoid and transverse sinus thrombosis (Fig. 1).

Screening tests for a thrombophilic state were within normal amounts. Given that the patient had lymphopenia and low oxygen saturation, the chest CT was done which showed ground glass opacity (Fig. 2), also the real time PCR-test for COVID-19 was positive. Considering the diagnosis, he underwent anticoagulant, Levetiracetam, hydroxychloroquine and Co-amoxiclav. At day 10, he was discharged with good health. Patient's written consent was obtained for publication.

3. Discussion

Coronaviridae members can cause neurological disease [5] but there are few studies about neurologic complications of COVID-19. ACE2 was identified as the receptor for COVID-19, which is present in nervous system and skeletal muscles so this virus infect these systems as well as the respiratory tract

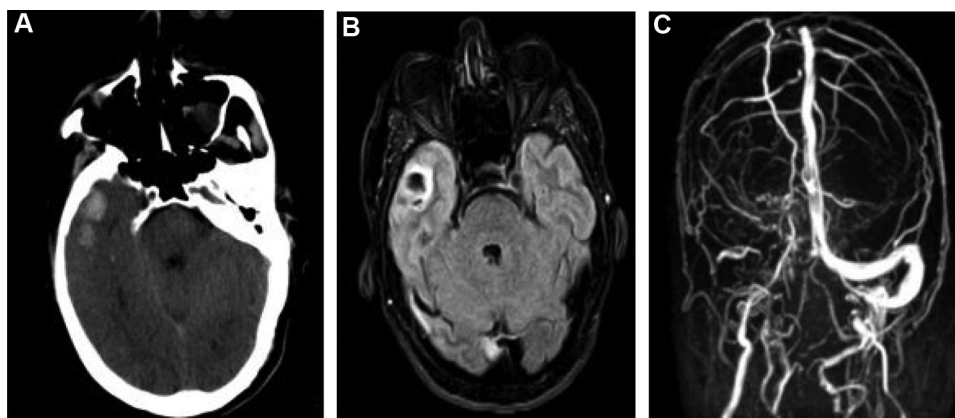


Fig. 1 – A.computed tomography (CT) image showed hemorrhage in right temporal lobe B. Fluid-attenuated inversion recovery images showed hemorrhagic infarct. C. Magnetic resonance venography demonstrates right sigmoid and transverse sinus thrombosis.