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Case Report

Fulminant cerebral edema as a lethal manifestation of COVID-19

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ABSTRACT

The contribution of neurological symptomatology to morbidity and mortality after infection with Severe Acute Respiratory Syndrome-associated Coronavirus (SARS CoV II) is ill-defined. We hereby present a case of a 57-year old male patient, in excellent physical condition, who was admitted to the Intensive Care Unit (ICU), with respiratory distress duo to SARS CoV II-induced bilateral pneumonia. After 2 weeks at the ICU, with respiratory conditions improving, the patient developed lethal cerebral edema. This case advocates regular wake-up calls in Coronavirus disease 2019 patients for neurological (radiological) evaluation to provide rapid diagnosis and a therapeutic window for fulminant central nervous system complications.

Introduction

In December 2019, human infection with a newly identified Severe Acute Respiratory Syndrome-associated Coronavirus (SARS CoV) was first reported from Wuhan, China [1]. In the spring of 2020, the world witnessed a major outbreak of the virus which causes Coronavirus disease 2019 (COVID-19). With the continuing SARS CoV 2 epidemic, Intensive Care Units (ICU) around the world face a substantial increase in patients requiring ventilatory support. Morbidity and mortality due to COVID-19 is largely attributed to respiratory distress after onset of bilateral pneumonia. The contribution of the nonrespiratory symptomatology of COVID-19 to prognosis is currently unclear. As shown by a recent case series, the presenting symptomatology of an infection with SARS CoV II can include gastrointestinal symptoms, eg, diarrhea or vomiting, as well as neurological manifestations including headache, anosmia, and dizziness [2-4]. While recent editorials call for enhanced clinical concern for central nervous system (CNS) pathology within the course of SARS CoV 2 infection, a direct correlation between an infection with this viral agent and neurological

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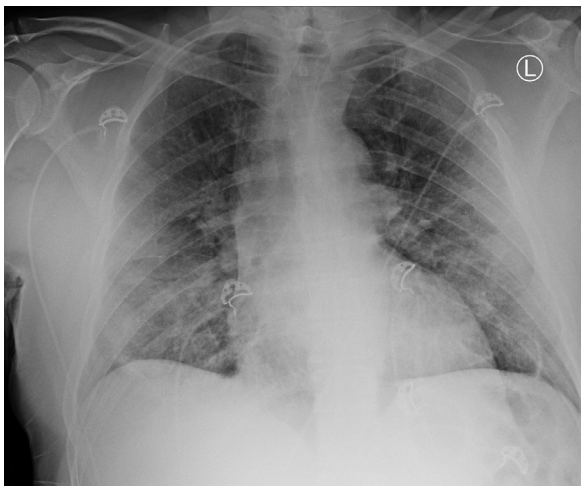

Fig. 1 – Chest X-ray on admission showing bilateral infiltrates compatible with COVID-19.

morbidity remains unclear [5-7]. We present a case of extensive cerebral edema in an ICU patient with hypoxic respiratory distress, caused by COVID-19 bilateral pneumonia.

Case report

On March 18, 2020 a 57-year-old male presented to our hospital. His medical history noted hypertension and his body mass index was 28 kg/m^2. He was in an excellent physical condition and was regular swimmer. The patient developed fatigue and fever after a trip to Austria on March 9. Over the course of a few days his symptoms worsened with dyspnea, nausea, vomiting, and diarrhea. He presented at the emergency department with acute respiratory distress, with tachypnea (40 breaths/min), arterial desaturation (88%), and an arterial blood gas analysis with a p_aO_2 level of 47 mm Hg. Oxygen therapy was administered using a nonrebreathing mask. Chest X-ray showed diffuse bilateral infiltrates (Fig. 1) and polymerase chain reaction on a nasopharyngeal swab tested positive for SARS CoV 2. Inflammatory parameters on admission were high, with C-reactive protein (CRP) of 303 mg/L (reference range: 0-10 mg/L) and white-cell count of 10.2 $\times$ 10^9/L (reference range: 4-10 $\times$ 10^9/L). On admission to the ICU, the patient was immediately intubated for respiratory failure due to Acute Respiratory Distress Syndrome (ARDS). He also developed acute kidney injury for which continuous renal replacement therapy was initiated. After 7 days on the ICU, a CT scan of the thorax was indicated as the ARDS persisted, showing bilateral pulmonary emboli despite prophylaxis with low-molecular weight heparin (LMWH). Therapeutic LMWH was subsequently started (10.000IE, twice daily) instead of prophylactic dosage. During the first 2 weeks of ICU admission the patient was managed on mechanical ventilation requiring high dosages of sedatives (midazolam) and intermittent neuromuscular blockade with rocuronium. Intermittent prone positioning was done during the first week of admission. The clinical course was further characterized by hemodynamic stability, requiring low dose norepinephrine. Lactate levels remained normal. During the second week, respiratory condition markedly improved as indicated by improved p_aO_2/f_iO_2 ratio, and ventilator settings improved to assisted-breathing and sedatives could tapered. On day 15, approximately 24 hours after midazolam sedation had been stopped, dilated and nonreactive pupils were noted on physical examination. An emergency CT scan and CT angiography of the brain showed extensive cerebral edema and brain herniation (Figs. 2 and 3). Several subcortical hemorrhages were present without focal areas of arterial

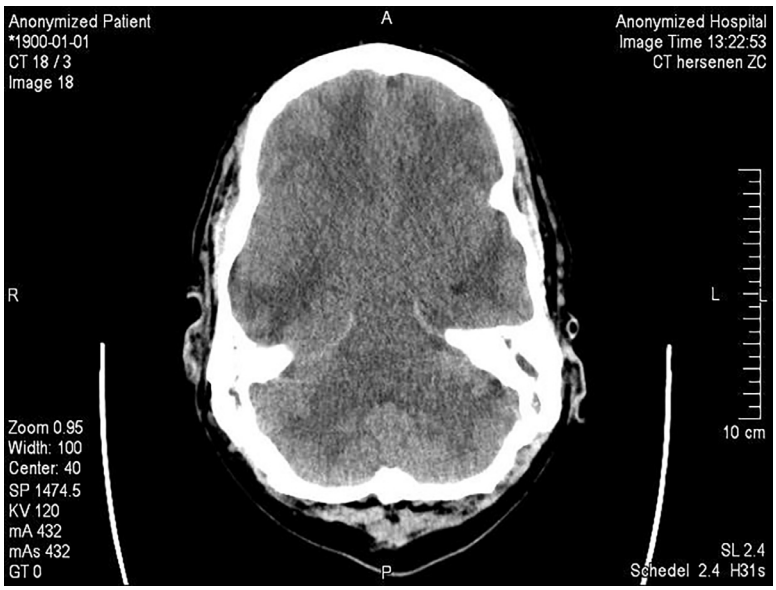

Fig. 2 – Transversal cerebral CT scan showing extensive vasogenic edema and herniation of temporal lobes toward the brain stem with obliteration of basal cerebral cisterns.

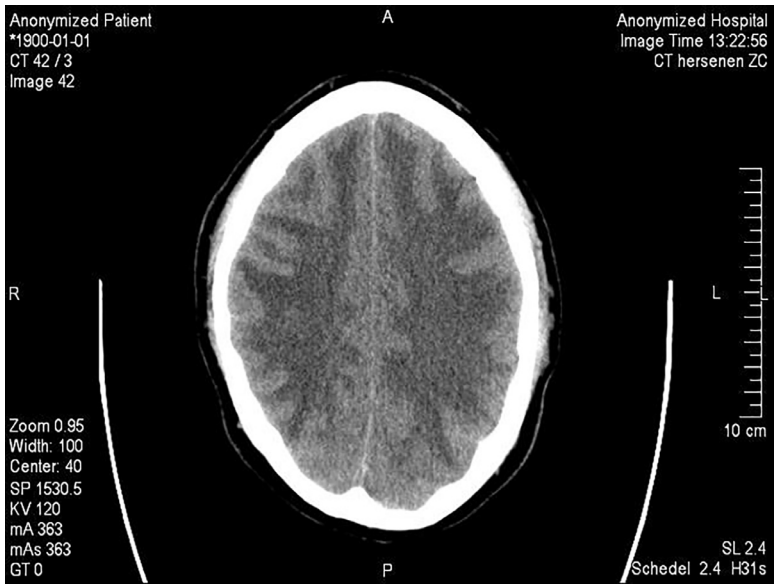

Fig. 3 – Transversal cerebral CT scan showing extensive vasogenic edema with effacement of ventricles and peripheral sulci and gyri.

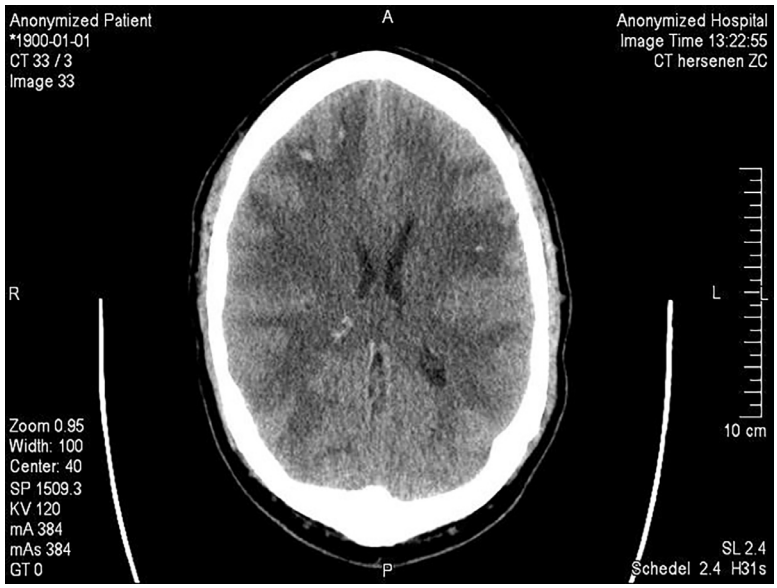

Fig. 4 – Transversal cerebral CT scan showing multiple juxtacortical microbleeds, which may be compatible with venous hemorrhagic infarction.

infarction (Fig. 4). CT angiography showed absence of cerebral perfusion distally from the internal carotid arteries. The patient had remained in a hypercoagulable state, despite the administration of therapeutic dosages of LMWH, as was confirmed by thromboelastometry (Supplementary Fig. 1) with a modestly elevated fibrinogen level of 5.7 g/L (reference range: 2.0-4.0 g/L). Partial thromboplastin time was normal and activated partial thromboplastin time was 25 seconds (reference range: 25-31 seconds). Brain stem reflexes on subsequent clinical neurological examination were absent. Given the infaust prognosis, further treatment was considered futile and the patient died shortly afterward. The patient's relatives granted consent for publication of his case, autopsy was not performed.

Discussion

The observed signs and symptoms of COVID-19, likely due to a direct inflammatory response in the respiratory tract, in-

clude cough, dyspnea and fever. SARS CoV infections target the angiotensin-converting enzyme 2 receptor and thereby gain entry to the human body to replicate [8]. During earlier coronavirus outbursts, including during the Middle East respiratory syndrome coronavirus outbreak in 2012, reports have been published on coronavirus spreading to the CNS by directly infestation of the CNS [9-12]. Several hypotheses on CNS infiltration have been formulated, including viral transmission from the nasal cavity via the olfactory nerve [13], but a recent report did not find direct viral CNS entry [14]. We hereby present a case of massive and rapidly fatal cerebral edema in a patient who was admitted to the ICU with severe ARDS due to COVID-19. In this case, the absence of histopathological evidence or cerebrospinal fluid analysis complicates determination of a certain diagnosis. The differential diagnosis in this case includes: (massive) cerebral venous sinus thrombosis, hemorrhagic/necrotizing (viral) encephalitis (and thereby developing reactive cerebral edema) and (massive) vasculitis [15]. SARS CoV 2 is the latest descendent in the strain of coronaviruses, with prior fellow species suggested to (directly) cause necrotizing encephalitis. CT scan showed multiple juxtacortical hemorrhages (Fig. 4), which may well fit the diagnosis of cranial sinus thrombosis. Remarkably, cortex involvement was limited, making arterial infarction less suspect as a cause for cerebral vasogenic edema. Of note, hypercoagulability in COVID-19 has recently been well described and was present in this patient despite treatment with therapeutic LMWH [16].

Conclusion

Details of CNS manifestations of COVID-19 caused by SARS CoV 2 infection are ill-defined and uncertain. However, based on clinical observations and research on prior coronaviruses, the potential of SARS CoV 2 to involve CNS tissue should be considered. The course of events in this case advocates wake-up calls on a regular basis to evaluate cerebral function and to consider thorough neurological evaluation, including CT angiography. In this case earlier detection might have been possible and therapeutic options could have theoretically included endovascular thrombectomy for cerebral venous sinus thrombosis or corticosteroids for cerebral vasculitis.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.radcr.2020.06.053.

REFERENCES

[1] Lu H, Stratton CW, Tang YW. Outbreak of pneumonia of unknown etiology in Wuhan, China: the mystery and the miracle. J Med Virol 2020;92(4):401–2.

[2] Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020;395(10223):507–13.

[3] Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA 2020;323(11):1061–9. doi:10.1001/jama.2020.1585.

[4] 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;77(6):683–90. doi:10.1001/jamaneurol.2020.1127.

[5] Zhou L, Zhang M, Wang J, Gao J. Sars-Cov-2: underestimated damage to nervous system. Travel Med Infect Dis 2020;10:1642. doi:10.1016/j.tmaid.2020.101642.

[6] Li YC, Bai WZ, Hashikawa T. The neuroinvasive potential of SARS-CoV2 may play a role in the respiratory failure of COVID-19 patients. J Med Virol 2020;92(6):552–5. doi:10.1002/jmv.25728. Epub 2020 Mar 11.

[7] Turtle L. Respiratory failure alone does not suggest central nervous system invasion by SARS-CoV-2. J Med Virol 2020;92:705–6.

[8] To KF, Lo AW. Exploring the pathogenesis of severe acute respiratory syndrome (SARS): the tissue distribution of the coronavirus (SARS-CoV) and its putative receptor, angiotensin-converting enzyme 2 (ACE2). J Pathol 2004;203(3):740–3.

[9] Arabi YM, Harthi A, Hussein J, Bouchama A, Johani S, Hajeer AH, et al. Severe neurologic syndrome associated with Middle East respiratory syndrome corona virus (MERS-CoV). Infection 2015;43(4):495–501.

[10] Gu J, Gong E, Zhang B, Zheng J, Gao Z, Zhong Y, et al. Multiple organ infection and the pathogenesis of SARS. J Exp Med 2005;202(3):415–24.

[11] Xu J, Zhong S, Liu J, Li L, Li Y, Wu X, et al. Detection of severe acute respiratory syndrome coronavirus in the brain: potential role of the chemokine Mig in pathogenesis. Clin Infect Dis 2005;41(8):1089–96.

[12] Arbour N, Day R, Newcombe J, Talbot PJ. Neuroinvasion by human respiratory coronaviruses. J Virol 2000;74(19):8913–21.

[13] Dube M, Le Coupanec A, Wong AHM, Rini JM, Desforges M, Talbot PJ. Axonal transport enables neuron-to-neuron propagation of human coronavirus OC43. J Virol 2018;92(17):404–18.

[14] 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;382(23):2268–70.

[15] 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;20:1187. doi:10.1148/radiol.2020201187.

[16] Terpos E, Ntanasis-Stathopoulos I, Elalamy I, Kastritis E, Sergentanis TN, Politou M, et al. Hematological findings and complications of COVID-19. Am J Hematol 2020;95:834–47.