

CASE REPORT

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COVID-19 masquerading as a non-convulsive status epilepticus

Sofie Moorthamers^{1*}, Thierry Preseau¹, Saïd Sanoussi² and Marie-Dominique Gazagnes³

Abstract

Since the outbreak of the coronavirus disease 2019 (COVID-19) pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), more and more atypical presentations of COVID-19 are being reported. Here, we present and discuss non-convulsive status epilepticus (NCSE) as presenting symptom of SARS-CoV-2 infection at the Emergency Department.

Keywords: Non-convulsive status epilepticus, COVID-19 atypical ED presentations, Reversible clinical picture of SARS-CoV-2 infection, EEG availability at ED

Introduction

The outbreak of SARS-CoV-2 in Wuhan, Central China, in January 2020, has resulted in a global pandemic with significant morbidity and mortality [1]. At the beginning of the pandemic, COVID-19 was primarily considered a pulmonary disease; however, the clinical spectrum of SARS-CoV-2 infection is very broad and extrapulmonary involvement is increasingly cited in literature. Various neurological presentations have been linked to SARS-CoV-2, but only a few recent reports have described non-convulsive status epilepticus (NCSE) as the first manifestation of SARS-CoV-2 infection [2–4]. Especially when seen in conjunction with other underlying diseases, NCSE often goes unrecognized and NCSE is commonly underdiagnosed in the Emergency Department (ED) and intensive care unit (ICU). However, failure and delay to diagnose NCSE may cause inappropriate treatment and irreversible brain damage [5]. Therefore, it is critically important for the emergency physician to consider NCSE as a—if treated in a timely manner—completely reversible neurological picture of COVID-19 disease. In order to bring further awareness of NCSE as

a rare initial manifestation of COVID-19 disease, we here present a case of a SARS-CoV-2-associated NCSE in a 76-year-old-female presenting with unexplained coma at the ED.

Narrative/case presentation

A 76-year-old female was brought to the Emergency Department (ED) after being found unconscious at home with a recorded room air saturation of 86%. She had a past medical history significant for arterial hypertension, hypercholesterolemia, transient ischemic attack, and non-valvular atrial fibrillation. Home medications included apixaban, digoxin, atorvastatin, nebivolol, perindopril, moxonidine, and esomeprazole. There was no previous smoking, alcohol, or illicit drug use. According to her relatives, she was last seen well 3 h earlier. She had presented no fever, cough, dyspnea, or preceding illness. At ED presentation, her blood pressure was 83/47 mmHg; heart rate, 90 beats per minute; respiratory rate, 12 breaths per minute; oxygen saturation, 100% on high flow oxygen via a non-rebreather mask; and temperature, 35°C. An arterial blood gas indicated a type 1 respiratory failure (Table 1). On examination, she was completely unresponsive (Glasgow Coma Scale score of 3) with no tonic-clonic activity. Deep tendon reflexes were weak, and Babinski's sign was bilaterally present.

* Correspondence: sofie.moorthamers@chu-brugmann.be; moorthamers.sofie@gmail.com

¹Emergency Department, Brugmann University Hospital, Université Libre de Bruxelles, Brussels, Belgium

Full list of author information is available at the end of the article



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Table 1 Patient data at the time of presentation to the Emergency Department

Value (normal range)	
<i>Venous blood puncture</i>	
Hemoglobin, g/dL (12.0–16.0)	13.4
White cell count, $\times 10^9/L$ (3.5–11)	8.07
Neutrophil count, $\times 10^9/L$ (1.50–6.70)	6.44
Lymphocyte count, $\times 10^9/L$ (1.20–3.50)	0.95
Platelet count, $\times 10^9/L$ (150–440)	202
C-Reactive Protein, mg/L (<5.0)	56.3
D-Dimer, ng/mL (0–500)	7393
PT, seconds (9.9–11.8)	11.8
APTT, seconds (21.6–28.7)	24
Anti-Factor Xa activity, U anti-Xa/mL	1.06
Sodium, mmol/L (136–145)	130
Potassium, mmol/L (3.4–4.4)	3.8
Chloride, mmol/L (98–107)	89
Bicarbonate, mmol/L (23–29)	27
Urea, mg/dL (17–48)	60
Creatinine, mg/dL (0.50–0.90)	1.73
Serum glucose, mg/dL (70–100)	142
Alanine transaminase, U/L (<33)	19
Creatine kinase, U/L (26–192)	2376
Myoglobin, mcg/L (<58)	6063
Lactate, mmol/L (0.7–2.0)	1.6
Ammonia, mcg/dL (18.7–86.9)	21
Bioactive monomeric prolactin, mcg/L (3.5–18.0)	29.4
TSH, mU/L (0.27–4.20)	3.78
Peripheral venous blood culture set (2 independent sets)	Negative
<i>Arterial blood puncture at ED admission (FiO₂ 100%)</i>	
pH (7.35–7.45)	7.47
pCO ₂ , mm Hg (32–45)	35
pO ₂ , mm Hg (75–104)	234
P/F ratio (>300)	234
Saturation O ₂ , % (95–98)	100
Carboxyhemoglobin, % (<1.0)	0.9
Methemoglobin, % (<0.5)	0.7
<i>Arterial blood puncture at ICU admission (FiO₂ 40%)</i>	
pH (7.35–7.45)	7.48
pCO ₂ , mm Hg (32–45)	35
pO ₂ , mm Hg (75–104)	102
P/F ratio (>300)	255
Saturation O ₂ , % (95–98)	98
<i>CSF examination</i>	
CSF macroscopic examination	Crystal clear
CSF opening pressure, cmH ₂ O	-
CSF red cell, $\times 10^9/L$ (0–5)	0.1

Table 1 Patient data at the time of presentation to the Emergency Department (*Continued*)

Value (normal range)	
CSF white cell, $\times 10^9/L$ (0–5)	2.8
CSF glucose, mg/dL (45–80)	75.8
CSF protein, g/L (0.15–0.45)	0.44
CSF oligoclonal bands	-
CSF lactate, mmol/L (1.11–2.44)	3.76
CSF PCR for SARS-CoV2	Negative
CSF FilmArray Meningitis/Encephalitis Panel*	Negative
CSF PCR for Herpes Simplex 1	Negative
CSF bacterial and fungal culture	Negative
CSF antinuclear antibodies	Negative
Antibodies against NMDAR, LGI1, CASPR2, GABA-B1/B2, DPPX, AMPA1/2 in serum, and CSF	Negative
Paraneoplastic anti-neuronal antibodies in serum and CSF	Negative
<i>Urine analysis</i>	
Leucocytes/ μL (<10)	26
Erythrocytes/ μL (<12)	26
Epithelial cells	Absent
Hyalin casts	+++
Crystals	Absent
Bacteria	+
Fungi	Absent
Urine culture set	Negative

PT prothrombin time, APTT activated partial prothrombin time, TSH thyroid stimulating hormone, CSF cerebrospinal fluid, NMDAR N-methyl-D-aspartate receptor, LGI1 leucine-rich glioma inactivated 1, CASPR2 contactin-associated protein 2, GABA-B γ -Aminobutyric acid-B receptor, DPPX dipeptidyl aminopeptidase-like protein 6, AMPA1/2 GluR1 and GluR2 subunits of the AMPA receptor; Paraneoplastic antibodies included anti-Hu, anti-Yo, anti-Ri, and anti-amphiphysin

**Escherichia coli* K1, *Haemophilus influenzae*, *Listeria monocytogenes*, *Neisseria meningitidis*, *Streptococcus pneumoniae*, *Streptococcus agalactiae*, cytomegalovirus, enterovirus, herpes simplex virus 1 and 2, human herpesvirus 6, human parechovirus, varicella-zoster virus, and *Cryptococcus neoformans*/*Cryptococcus gattii*

Chest auscultation revealed bibasilar coarse crackles. The remainder of her physical examination was non-contributory. Brain computed tomography (CT) and subsequent CT angiography were normal. CT of the chest and abdomen showed ground glass opacities, predominantly peripheral and involving all five lung lobes, compatible with COVID-19 pneumonia (Fig. 1). Baseline blood analysis was notable for lymphopenia, rhabdomyolysis, crush-related acute kidney injury, and elevated prolactin level (Table 1). A nasopharyngeal swab real-time reverse-transcriptase-polymerase-chain-reaction (rRT-PCR) test was positive for SARS-CoV-2. The blood and urine cultures were negative. Cerebrospinal fluid examination was unremarkable, except for elevated lactate (Table 1). To secure her airway and assure adequate oxygenation, rapid sequence intubation using ketamine 1–2 mg/kg and succinylcholine 1.5 mg/kg was performed and mechanical ventilation started. A bolus of 10 mg midazolam was administered. Norepinephrine titrated up to 0.4 mcg/kg/min was added for refractory hypotension after 30 mL/kg of intravenous crystalloid fluid resuscitation, targeting a mean arterial pressure of 65 mmHg. She received intravenous ceftriaxone 2g and

dexamethasone 6mg as recommended for severe COVID-19 pneumonia. As urgent electroencephalography (EEG) is not routinely available at our ED, EEG could not be obtained. With NCSE as presumed etiology of the patient's coma, she was empirically treated with intravenous valproic acid 40 mg/kg and admitted to the intensive care unit (ICU). The EEG at day 1 showed non-epileptiform generalized background slowing, consistent with antiepileptic drug (AED) treatment. The next 2 days on the ICU, the patient's clinical condition improved (Glasgow Coma Scale score of 15) due to expected AED responsiveness. At day 4, after being extubated, brain magnetic resonance imaging (MRI) was performed and confirmed NCSE as a cause of her unexplained coma at the ED, showing multifocal bilateral cortical hyperintensities on diffusion weighted images (DWIs) with decreased apparent diffusion coefficient (ADC) and increased signal in T2 and FLAIR with no arterial distribution (Fig. 2). These signal changes, that do not respect vascular territories and are usually reversible over days, typically result from seizure activity, and represent regional vasogenic and cytotoxic edema, reflecting peri-ictal hemodynamic and metabolic changes,

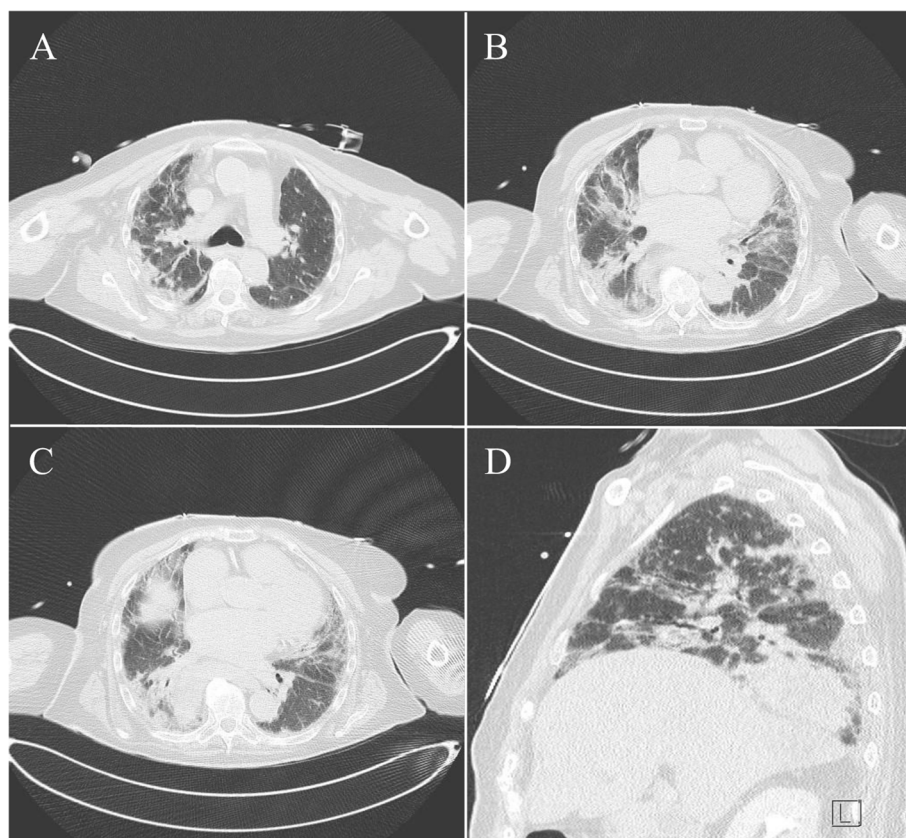


Fig. 1 Patient's chest CT showing ground glass opacities, predominantly peripheral, involving the five lung lobes, compatible with severe COVID-19 pneumonia. **A–C** Axial view. **D** Sagittal view

respectively. At day 5, she left the ICU and 7 weeks later, she was discharged home from our COVID-19 neuro-rehabilitation unit, in excellent condition and without neurological deficit. Repeat brain MRI showed complete regression of previously described imaging changes and absence of any type of lesion.

Discussion

Since the onset of the COVID-19 pandemic, a variety of possible neurological manifestations due to SARS-CoV-2 infection have been reported, including, but not limited to, anosmia, dysgeusia, stroke, infectious and autoimmune meningoencephalitis, acute necrotizing encephalopathy, acute disseminated encephalomyelitis, posterior reversible encephalopathy, and Guillain-Barre syndrome [1, 2]. Up to now, only a relatively low number of cases with new onset seizures or status epilepticus in the context of COVID-19 have been published [6–9]. Here, we report a case of NCSE as presenting symptom of a SARS-CoV-2 infection at the ED in a patient with no previous history of epilepsy. Although recently multiple reports of generalized tonic-clonic seizures and one report of focal status epilepticus as initial presentation of COVID-19 at the ED have been described, NCSE as

initial presentation of SARS-CoV-2 infection at the ED has been rarely reported [3, 4, 9, 10]. NCSE refers to an electro-clinical state of prolonged non-convulsive seizure activity that manifests primarily as a sudden alteration of consciousness [11]. EEG often—and even more during the COVID-19 pandemic—being unavailable, non-convulsive seizures frequently go unrecognized at the ED; this may have deleterious consequences as NCSE is a critical emergency associated with substantial mortality (25–30%) and irreversible brain damage if not managed in a timely manner [11, 12]. Although pathophysiological mechanisms underlying ictogenesis in SARS-CoV-2 infection remain to be understood. Viral encephalitis and direct invasion of SARS-CoV-2 in the brain may be one of the provoking factors for seizure [9, 13]. In addition, severe COVID-19 disease can result in metabolic and electrolyte imbalances, hypoxia, and cerebrovascular events, all known to facilitate epileptogenesis [9, 13]. SARS-CoV-2 infection also may trigger a “cytokine storm” with rapid release of pro-inflammatory cytokines leading to systemic hyper-inflammation, brain damage, and seizures [13, 14]. In this particular case, with no precipitating factors other than hypoxia-induced facilitation of seizure present, we suggest whether the NCSE in our

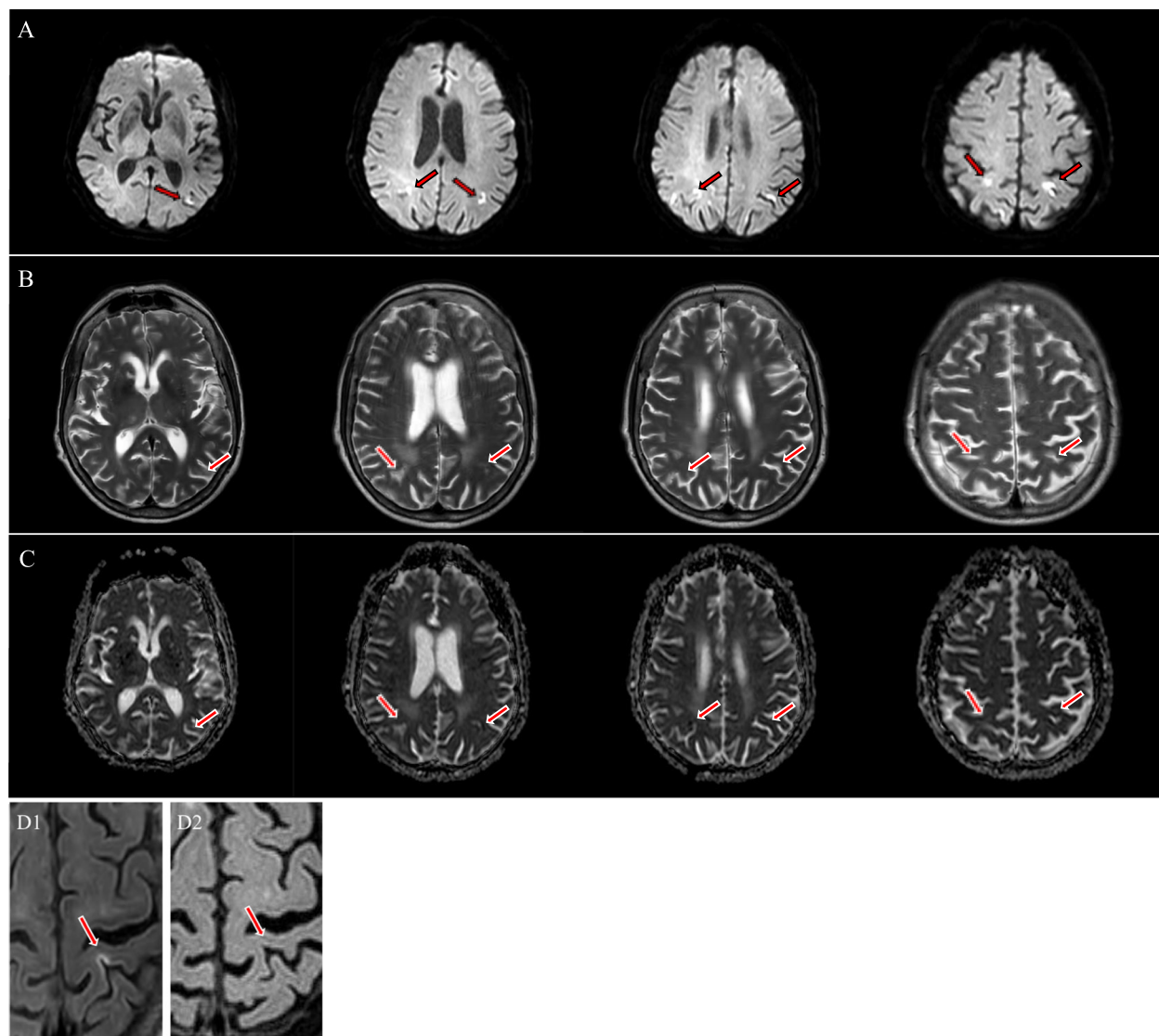


Fig. 2 Initial brain MRI: arrows show the focal cortical signal hyperintensity changes on diffusion weighted (**A**) and T2 weighted images (**B**) with reduced apparent diffusion coefficient on ADC map (**C**). Lesions are located in the cortical gray matter and lack arterial distribution. They are topographically compatible with transient postictal MRI changes indicating the presence of cytotoxic and vasogenic edema. Follow-up MRI revealed complete resolution of signal changes and no new other lesions. **D** FLAIR signal hyperintensity on initial brain MRI (D1) and normalized FLAIR signal intensity on follow-up MRI illustrating the reversibility of postictal MRI abnormalities (D2)

patient was indeed provoked by the “cytokine storm” associated with COVID-19. It highlights NCSE should not be overlooked in patients with SARS-CoV-2 infection—especially in the elderly—presenting with altered mental status. As mentioned, both delay to diagnosis and longer duration of NCSE are associated with increased morbidity and mortality [11, 12]. Therefore, even in the absence of electroencephalographic evidence to support the diagnosis of NCSE, AED initiation should—in our opinion—not be delayed in clinical suspected NCSE at the ED. Noteworthy, in our patient prompt NCSE recognition and treatment—before any EEG obtained—led to a

phenomenal and complete neurological recovery within 48 h. Besides the corresponding clinical picture, transient postictal imaging changes on brain MRI did allow us to retrospectively attribute the definite diagnosis of NCSE in our patient (Fig. 2) [13, 15–17]. This case alerts to the existence of a complete reversible picture of NCSE in SARS-CoV-2 patients and stresses the importance of doing “whatever it takes”—even in the elderly—albeit the clinical situation encountered at the ED initially may appear a perfect storm. Additionally, although NCSE occurs frequently in critical care patients (8–37%), surprisingly few reports mention potential NCSE

in COVID-19 ICU patients [12]. Therefore, to conclude, we focus attention on the predisposing context for NCSE in severe COVID-19 at the ICU and speculate that NCSE probably may be considered in certain ICU patients with persistently altered levels of consciousness, agitation, or spatial disorientation—before or after weaning of mechanical ventilation.

Conclusion

NCSE is a medical emergency, the morbidity, and mortality of which can be decreased by prompt recognition and treatment. NCSE as presenting symptom of COVID-19 at the ED has little been addressed so far. This case report highlights two important issues: first, emergency physicians should keep SARS-CoV-2 infection on their differential diagnosis as more atypical presentations are described, and second, it is important to consider NCSE in COVID-19 patients presenting with altered levels of consciousness at the ED and to not delay appropriate AED treatment. Last but not least, we suggest whether this clinical picture may need more attention at the COVID-19 ICU.

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Authors' contributions

Moorthamers Sofie: Conceptualization and writing—original draft preparation.
Preseau Thierry: Validation, supervision.
Sanoussi Said: Validation neuroimaging content.
Gazagnes Marie-Dominique: Validation, supervision, reviewing and editing.
The authors read and approved the final manuscript.

Declarations

Consent to participate

Informed consent was obtained from the patient for publication of this case report.

Competing interests

The authors did not receive any grant for this paper. The authors declare that they have no competing interests.

Author details

¹Emergency Department, Brugmann University Hospital, Université Libre de Bruxelles, Brussels, Belgium. ²Radiology Department, Brugmann University Hospital, Université Libre de Bruxelles, Brussels, Belgium. ³Stroke and Neurological Rehabilitation Department, Brugmann University Hospital, Université Libre de Bruxelles, Brussels, Belgium.

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