First motor seizure as presenting symptom of SARS-CoV-2 infection

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Dear Sir,

The SARS-CoV-2 pandemic is currently causing concern in the medical community as the virus is rapidly spreading around the world [1]. Since its identification in late December 2019 in China, the epidemiological picture is changing on a daily basis: in the last month, Italy has been the center of the European outbreak with a growing number of infected patients. Although patients with SARS-CoV-2 disease typically present with respiratory symptoms, pieces of information suggest that the virus may also have neurological manifestations [2]. We report a case of first motor seizure as presenting symptom of SARS-CoV-2 infection. The present case further underscores that initial manifestations of *novel Coronavirus* infection might be non-specific and it highlights the need for physicians to consider potential neurological manifestations of SARS-CoV-2 infection.

Case report

On February 28, 2020, a 54-year-old firefighter was admitted to our emergency room (ER) after a single seizure characterized by clonic movements in the right arm and loss of consciousness. His

relatives reported a sudden onset of involuntary and rhythmic movements involving the right hand and arm lasting about 1 or 2 min; after that, it was reported that the patient appeared generally stiffened and he lost consciousness. When he awakened, he was confused for about 30 min. At the ER admission, he reported suffering from conjunctivitis in the last 10 days and mild fever in the past week. He had no remote medical or neurological history; he had been taking ophthalmic steroids during the previous days but he was not under regular medications; there was no history of drug use. Vital parameters, peripheral oxygen saturation, and EKG were normal (body temperature 36.5 °C); neurological examination showed no focal deficits. Serum laboratory tests revealed neutrophilia (85.5%, NR 40–75%), normal white blood cell count ($6.38 \times 1000/\mu\text{L}$, NR 4.0–10.0), lymphopenia ($0.69 \times 1000/\mu\text{L}$, NR 0.8–4.0), normal serum sodium (140.8 mmol/L, NR 132.0–146.0), slightly elevated CRP (1.29 mg/dL, NR 0–0.5), and AST and ALT enzymes (57 and 59 UI/L respectively, NR 2–40 and 4–49). Head CT scan was unremarkable (Fig. 1a). Chest X-ray showed a single lingular disventilatory band (Fig. 1b). Urinalysis test, urine culture, and urinary antigen tests for *Streptococcus pneumoniae* and *Legionella pneumophila* were normal. The patient's electroencephalogram recorded the following day showed no abnormalities (Fig. 1c). In the suspicion of *Mycoplasma pneumoniae* infection, Azithromycin 500 mg QD for 3 days was prescribed. On February 29, the patient was discharged and a diagnosis of “first focal motor seizure” was made; no anti-epileptic medications were prescribed. After 4 days, on March 4, the patient was admitted to the ER again reporting cough, high fever, and shortness of breath; his daughter also had a high fever. His temperature was 38.5 °C, the heart rate was 100 bpm, and the peripheral oxygen saturation was 94%. Lab tests showed raised inflammatory markers; chest X-ray pointed out the appearance of mild bilateral perihilar consolidations (Fig. 1d); chest HR-CT scan showed bilateral ground-glass opacities (Fig. 1e). Based on epidemiological data and according to the government guidelines, two nasopharyngeal swabs were obtained and were found to be positive for SARS-CoV-2 on qRT-PCR. The patient was hospitalized in the Intermediate Care Unit and non-invasive ventilation (NIV) was undertaken. He

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Fig. 1 Chest x-rays, chest HRCT, brain CT scan, and EEG findings. Brain CT scan did not show any abnormalities (a). First chest x-ray performed on February 28th showed a lingular disventilatory band (b). Electroencephalogram (EEG) did not show any abnormalities (c). Second

chest x-ray performed on March 4th showed the appearance of mild bilateral peri-hilar consolidations (d). Chest HRCT scan carried out on the same day of the second chest x-ray revealed bilateral peripheral ground-glass opacities (GGO) compatible with interstitial pneumonia (e)

completely recovered after 2 weeks of antiviral therapy (*Lopinavir-Ritonavir*); he remains seizure-free.

The consultant neurologist who had been in close contact with the patient during the first ER admission was isolated for clinical monitoring. She had no signs or symptoms of infection and she tested negative for *SARS-CoV-2*.

Discussion

Europe and the USA are currently facing the *SARS-CoV-2* pandemic. This is primarily a respiratory disease marked by cough, fever, and shortness of breath [3]. However, it has been suggested that it might have neurologic complications in some instances. A report from a Chinese hospital pointed out that frequent neurological symptoms are altered consciousness, skeletal muscle damage, and cerebrovascular diseases [2]. We are reporting a case of a patient suffering from a first seizure as a possible presenting symptom of *SARS-CoV-2* infection. The initial presentation of the *novel Coronavirus* can be non-specific [3]: retrospectively, the patient's initial exams (lymphocytopenia and chest X-ray disventilatory band) were consistent with manifestations of *SARS-CoV-2* infection [3]. Considering the temporal association between seizure onset and *novel Coronavirus* infection, we hypothesize that this infection might have been responsible for the development of seizures in this patient. We speculate that the suggested *SARS-CoV-2*-induced "cytokine storm syndrome" [4] may have contributed to seizures onset, considering the

normality of both the serum sodium level and the peripheral saturation at the time of first hospitalization [5].

One limitation of this case is the absence of *SARS-CoV-2* testing on the first admission. Considering the previous history of mild fever and conjunctivitis, it is likely that the patient suffered from *SARS-CoV-2* infection even at the time of the first hospital admission. Secondly, the differential diagnosis included a cardiac syncope: our patient, however, did not suffer from any heart diseases, he was not performing any physical activity at the time of seizure onset, and he had a long recovery time when he awakened; moreover, his EKG and blood pressure were normal during the first hospital admission. Finally, we have not yet performed a brain MRI. The patient's neurological examination, however, was normal both before and after the seizure with no clinical deficits possibly related to brain lesions; the brain CT, moreover, showed no focal abnormalities.

In conclusion, this case *only* suggests a possible association between seizures onset and *SARS-CoV-2* infection and it points out the need to consider potential neurological symptoms of the *novel Coronavirus*; further cases with epidemiological data will clarify if the association is accidental or causative. This case also highlights the need for clinicians to be alert to *SARS-CoV-2* neurological complications. This is important both for patients and for neurologists. On the one hand, patients need to be quickly and accurately diagnosed in order to avoid delayed diagnoses and to prevent further transmission; on the other hand, neurologists must be protected from the risk of contracting the *SARS-CoV-2* infection even in non-specific situations.

Authors' contributions • Antonio Fasano: Design and conceptualized study; major role in the acquisition of data; analyzed the data; drafted the manuscript for intellectual content.

• Francesco Cavallieri: Major role in the acquisition of data; interpreted the data; revised the manuscript for intellectual content.

• Elena Canali: Acquisition of data; interpreted the data; revised the manuscript for intellectual content.

• Franco Valzania: Design and conceptualized study; interpreted the data; revised the manuscript for intellectual content.

All authors have approved the final article.

Data availability Dr. Fasano as the corresponding author has full access to all the data (data transparency).

Compliance with ethical standards

Conflict of Interest The authors declare that they have no conflict of interest.

Ethical approval Not applicable.

Consent to participate Not applicable.

Consent for publication Written informed consent was obtained from the patient for publication.

Informed consent The patient gave his informed consent for case description.

Code availability Not applicable.

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