COVID-19 and intracerebral haemorrhage: causative or coincidental?

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Abstract

Pneumonia appears to be the most common manifestation of coronavirus disease 2019 (COVID-19), but some extrapulmonary involvement, such as gastrointestinal, cardiac and renal, has been reported. The limited clinical data about the virus's behavior to date, especially extrapulmonary symptoms, suggest that we should be aware of the possibility of initial cerebrovascular manifestations of COVID-19.

Keywords: Central nervous system, COVID-19, extrapulmonary, intracerebral haemorrhage, involvement, symptoms
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Pneumonia appears to be the most common manifestation of the novel coronavirus disease 2019 (COVID-19), but some extrapulmonary involvement, such as gastrointestinal, cardiac and renal, has been reported [1–3]. The most common symptoms described to date include fever, cough, myalgia, fatigue and shortness of breath; in addition diarrhoea, chest pain, confusion, nausea and vomiting, headache, haemoptysis and hyposmia have been observed [4].

We present the case of a 79-year-old man with a history of fever and cough of 3 days' duration referred to the emergency department with acute loss of consciousness. At admission he was febrile (temperature 38.6°C), with a fast heart rate (115 beats per minute) and rapid breathing (respiratory rate, 22 breaths per minute). Blood pressure was 140/65 mm Hg. Partial pressure of oxygen was 51.8 mm Hg; partial pressure of carbon dioxide was 27.9 mm Hg; and saturated oxygen was 86.6%. There was no history of hypertension or anticoagulation therapy. In addition to loss of consciousness (Glasgow Coma Scale score = 7) and bilateral extensor plantar reflexes, physical examination revealed coarse rales in the left lower lobe of the lungs. Paraclinical findings revealed lymphopenia (590 cells/mm^2), erythrocyte sedimentation rate of 85 mm/h, C-reactive protein of 10 mg/L, creatinine of 1.4 mg/dL, platelets of 210 × 10^9/L, prothrombin time of 12 seconds, international normalized ratio of 1 and partial thromboplastin time of 64 seconds, as well as normal liver function and other routine laboratory tests. Lung computed tomography revealed a ground-glass opacity in the left lower lobe, and brain computed tomography revealed a massive intracerebral haemorrhage (ICH) in the right hemisphere, accompanied by intraventricular and subarachnoid haemorrhage (Fig. 1). Real-time PCR of oropharyngeal swab confirmed COVID-19 infection.

The question that thus arises is whether, according to the recent epidemic in our region (the Mazandaran province of Iran), COVID-19 infection causes ICH or whether it is a coincidental event with ICH. COVID-19 has been shown to use the angiotensin-converting enzyme (ACE) II receptor for cell entry [4]. ACE II is highly expressed in lung alveolar type 2 cells and epithelial cells of gastrointestinal system [1,4]. Angiotensin II receptors are also expressed in circumventricular organs and in cerebrovascular endothelial cells, which play a role in the regulation of multiple functions in the brain, including regulation of hormone formation and sympathoadrenal system, water and sodium intake, vascular autoregulation and cerebral blood flow [5]. Angiotensin II is a vasoconstrictor which has a proinflammatory effect [6]. Thus, it is reasonable to hypothesize that brain ACE II could be involved in COVID-19 infection and its dysfunction, leading to disruption of autoregulation as well as blood pressure spikes due to arterial wall rupture.

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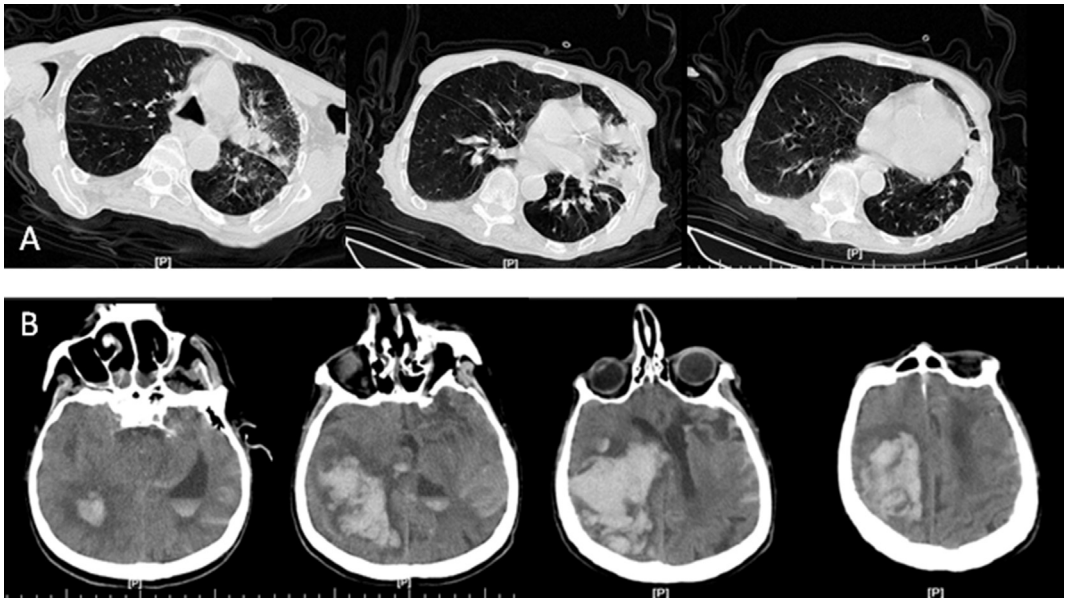

FIG. 1. (A) Spiral lung CT scan revealing ground-glass opacity in lateral and anteromedial segment of left inferior lobe. (B) Brain CT scan revealing massive intracerebral haemorrhage in right hemisphere accompanied by intraventricular and subarachnoid haemorrhage. CT, computed tomographic.

Another question that arises is how the virus invades the central nervous system. Anecdotal reports from specialists in Iran consistently report hyposmia or anosmia to be common, particularly in the early stage of infection. It is possible that COVID-19 directly invades the central nervous system via the olfactory receptors of cranial nerve I in the nasal cavity cell membrane. Although this is just a theory, in order to explain the limited clinical data regarding the virus's behavior up to now, especially extrapulmonary symptoms, we should be aware of the possibility of initial cerebrovascular manifestations of COVID-19.

Conflict of interest

The authors declared no potential conflicts of interest.

References

[1] Gu J, Han B, Wang J. COVID-19: gastrointestinal manifestations and potential fecal–oral transmission. Gastroenterology 2020. In press.
[2] Liu R, Ming X, Zhu H, Song L, Gao Z, Gao L, et al. Association of cardiovascular manifestations with in-hospital outcomes in patients with COVID-19: a hospital staff data. medRxiv 2020. https://doi.org/10.1101/2020.02.29.20029348.
[3] Lai CC, Shih TP, Ko WC, Tang HJ, Hsueh PR. Severe acute respiratory syndrome coronavirus (SARS-CoV-2) and corona virus disease-2019 (COVID-19): the epidemic and the challenges. Int J Antimicrob Agents 2020;55:105924.
[4] Sahin AR, Erdogan A, Agaoglu PM, Dineri Y, Cakirci AY, Senel ME, et al. 2019 novel coronavirus (COVID-19) outbreak: a review of the current literature. EJMO 2020;4:1–7.
[5] Saavedra JM. Brain angiotensin II: new developments, unanswered questions and therapeutic 49 opportunities. Cell Mol Neurobiol 2005;25:485–512.
[6] Klempin F, Mosienko V, Matthes S, Villela DC, Todiras M, Penninger JM, et al. Depletion of angiotensin-converting enzyme 2 reduces brain serotonin and impairs the running-induced neurogenic response. Cell Mol Life Sci 2018;75:3625–34.