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.

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Letter to editor: Severe brain haemorrhage and concomitant COVID-19 Infection: A neurovascular complication of COVID-19

Beyond pulmonary infection, SARS CoV can cause dysfunction of multiple other organs and systems. Cardiovascular complications after COVID-19 have now been reported very often but the knowledge on neurovascular complications especially brain haemorrhage is scars. Here, we report the first case of COVID-19 positive patient presenting with a concomitant subarachnoid haemorrhage from an intracranial aneurysm. A 60-year-old woman was admitted to our emergency department due to loss of consciousness. The patient was intubated due to reduced Glasgow Coma Scale (GCS) and respiratory insufficiency. A computer tomography (CT) with CT-angiography revealed left frontal haemorrhage with ventricle bleeding (Fig. 1 D, E) from a ruptured pericallosal artery aneurysm around 5 mm in size (Fig. 1C, F). Oropharyngeal swab with PCR based testing was COVID-19 positive. A chest CT confirmed pneumonia predominantly of left lung (Fig. 1 A, B). On admission laboratory diagnostic showed elevated troponin 45 ng/ml (normal < 14 ng/ ml) and creatine kinase 4920 U/l (normal < 145 U/l). Elevated CRP 1.1 mg /dl and leukocytes 14.2X1000 µl. Slightly elevated lactate dehydrogenase 360 U/l (normal < 247 U/l) and elevated liver enzyme GOT 103 U/I (normal < 31 U/l).

The aneurysm was clipped microsurgically immediately after admission. After clipping of the aneurysm, due to positive COVID-19 PCR, the patient was transferred to a COVID-19 specialized ward for the treatment of infection and for the further intensive medical care. Cerebrospinal fluid (CSF) diagnostic revealed no viral genome in the CSF. Initially elevated troponin was normalized in the further course and no cardiac complication occurred. CT perfusion studies on day 3, 6, 9 and 12 showed no signs of cerebral vasospasm. Until last imaging on day 12-post ictus no delayed cerebral ischemia was detected. Patient still needs the treatment of pneumonia. Due to poor grade subarachnoid haemorrhage (WFNS grad 4), the patient is completely cured from COVID-19 and now transferred for rehabilitation.

Involvement of other organs especially the brain and the cardiovascular system increase additional morbidity and mortality in COVID-19 infected patients. The elderly patients with chronic medical conditions are particularly at risk to develop neurological complications including olfactory and gustatory disturbances (Vavougios, 2020) and in some cases an encephalitis (Ye et al., 2020) showing the possible accessibility of the virus to the brain and involvement of central nervous system (Duong et al., 2020). Moreover, COVID-19 infection can pose emotional and psychological stress in affected patients (Chew et al., 2020).

This is the first case of COVID19 infection and concomitant aneurysmal subarachnoid haemorrhage from a ruptured pericallosal artery aneurysm. Whether COVID-19 infection led to aneurysm formation or rupture of an already existing aneurysm is still unexplored. There are however, multiple mechanisms, how an intracranial aneurysm can possibly lead to vascular wall instability during systemic inflammation due to viral infection. Viral infections including influenza A and COVID-19 are known to induce cytokine storm (hypercytokinemia) leading to elevated systemic inflammation with high levels of IL-6, IL-1β and TNFα (Muhammad et al., 2011; Qin et al., 2020). Systemic inflammation is known to cause vascular injury including breakdown of collagen and permeability of blood-brain barrier. Influenza A virus infection for example disturbs BBB through involvement of systemic elevated MMP-9 that breaks collagen present in the basal membrane of every arterial wall and a high collagen turnover in the systemic circulation is a sign of instability of existing intracranial aneurysm (Hackenberg et al., 2020) in patients with unruptured intracranial aneurysms. Moreover, COVID-19 infection has been reported to increase systemic inflammation through dysbalance of T helper cells with exaggerated Th1 response (Huang et al., 2020). Similar kind of alterations in T helper cells populations have been found in patients with intracranial aneurysms (Zhang et al., 2016). Moreover, a disturbed balance of macrophages and other inflammatory markers has been found in the wall of ruptured intracranial aneurysms (Hasan et al., 2012) showing that inflammation is an important component of instable aneurysms. In our patient, we found elevated systemic leukoctyes as a sign of systemic inflammation that is probably due to both infection and SAH. We however could not analyse subpopulations of different leukocytes in systemic circulation that might be altered. Another possibility could be a direct invasion of virus in the brain as previously reported (Duong et al., 2020). However, we did not find virus genome in the cerebrospinal fluid and consequently it is highly unlikely that virus had any direct influence.

Taken together, aneurysm instability partially due to systemic inflammation after virus infection might be one possible reason leading to SAH. This is however a single case report with concomitant SAH and COVID-19. Therefore, further epidemiological/clinical studies are needed to confirm the relationship and animal experiments in controlled conditions are required to find out exact mechanism.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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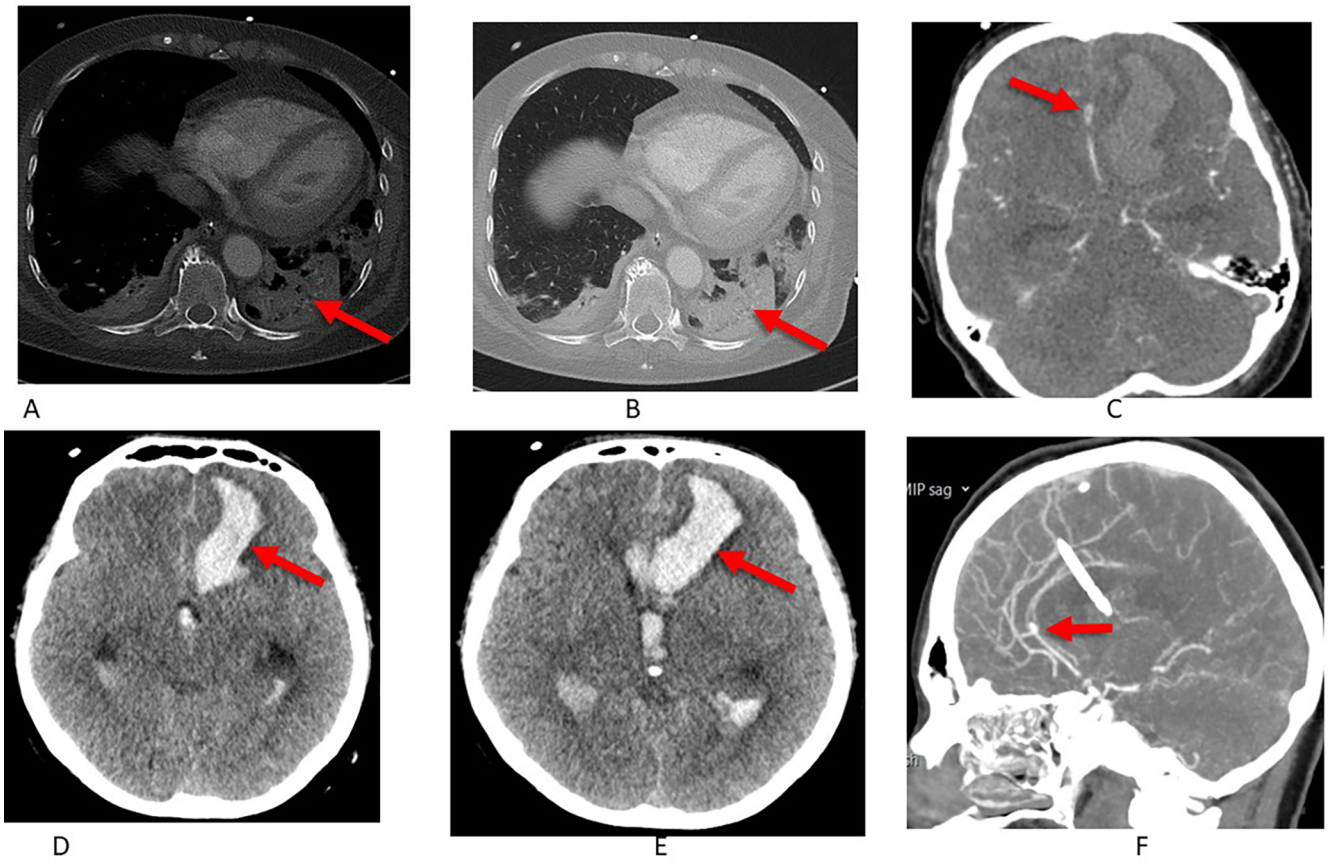

Fig. 1. Concomitant COVID-19 infection with pneumonia (A, B) and subarachnoid haemorrhage with intraventricular and intracerebral haemorrhage (C, D, E) from a pericallosal artery aneurysm (F).

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bbi.2020.05.015.

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