

Intracranial hemorrhage in coronavirus disease 2019 (COVI19)

Dr hadi ebrahimi

Faculty member of babol university medical sciences

Cerebrovascular Disease

Cerebrovascular disease – injury to the brain due to altered bloodflow due to **ischemia** or **hemorrhaging** → **Stroke**

- ▶ 3rd leading cause of death in the U.S. (following heart disease and cancer) and most prevalent neurologic disorder
- ▶ The brain is a highly aerobic tissue, requiring a constant supply of oxygen and glucose through the blood
 - ▶ **Hypoxia** – **impaired oxygenation** to the tissues by lowered PO_2 , impairment of the blood's oxygen-carrying capacity, or inhibition of O_2 use by the tissues
 - ▶ **Ischemia** – transient or permanent **interruption of normal circulatory bloodflow** due to a reduction in perfusion pressure (e.g., hypotension) or small-/large-vessel obstruction
 - ▶ **Global cerebral ischemia** – a **generalized reduction** of cerebral perfusion (e.g., **hypotension**)
 - ▶ **Focal cerebral ischemia** – follows a **reduction or cessation of bloodflow to a localized area** due to a small-vessel disease (e.g., vasculitis; occlusion secondary to arteriosclerotic lesions with hypertension) or large-vessel disease (e.g., embolic or thrombotic arterial occlusion associated with atherosclerosis)
 - ▶ **Infarction** – **necrosis** caused by impaired oxygenation from an obstruction to bloodflow
- ▶ **Hemorrhage** – results from ruptured blood vessels due to hypertension or aneurysms

the relationship between COVID-19 and cerebrovascular disease (CVD)

CVD has been associated with poor outcomes among COVID-19 patients .

subset of these patients develops CVD during the course of hospitalization

Whereas ischemic CVD, which has been attributed to a hypercoagulable state characterized by micro- and macrovascular thrombotic angiopathy

- **Age and sex distribution of COVID-19 patients with intracranial hemorrhage**
- **Majority** of the COVID-19 patients with intracranial hemorrhage were male (**65.8%**).
- The reported age of these patients ranged from **31 to 78** years. Across all case reports and case series, only **16%** of patients **were < 50 years** old. The mean or median age of the patients was > 50 years in all but one cohort study

Types of intracranial hemorrhage among COVID-19 patients

- Hemorrhage involving **multiple cranial** compartments (MCH) was reported in 14 cases (**9.5%**).

- compartments were involved

intraparenchymal hemorrhage (IPH) being the most **common** variety (**62.6%**),

SAH (15.0%)

SDH) (11.6%),

IVH) (1.4%).

In patients with IPH,

the **most location** of the bleed was the **cerebral lobes** (**93.5%**).

basal ganglia (**5.4%**)

cerebellum (1.1%).

Initial symptom (respiratory vs neurologic)

- Majority (71%) of the patients were **admitted** due to respiratory symptoms of COVID-19 and **developed** the intracranial hemorrhage (ICH) in their course of admission.
- The **interval between** the onset of respiratory symptoms and diagnosis of ICH ranged from **2 to 25 days**.
- The rest (21%) were admitted due to neurological symptoms, such as acute loss of consciousness and sudden onset severe headache, and were later confirmed to have COVID-19 through RT-PCR tests.

Comorbid conditions in the COVID-19 patients with intracranial hemorrhage

hypertension

diabetes mellitus (DM)

hyperlipidemia

, coronary artery disease (CAD)

obesity

congestive heart failure (CHF)

obstructive sleep apnea (OSA)

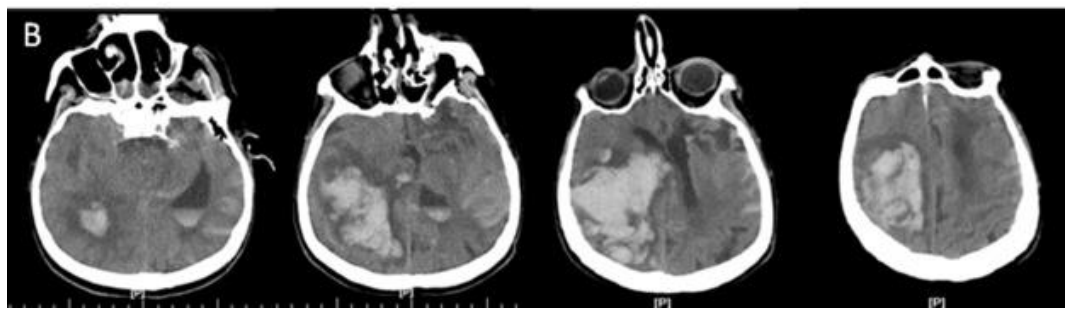
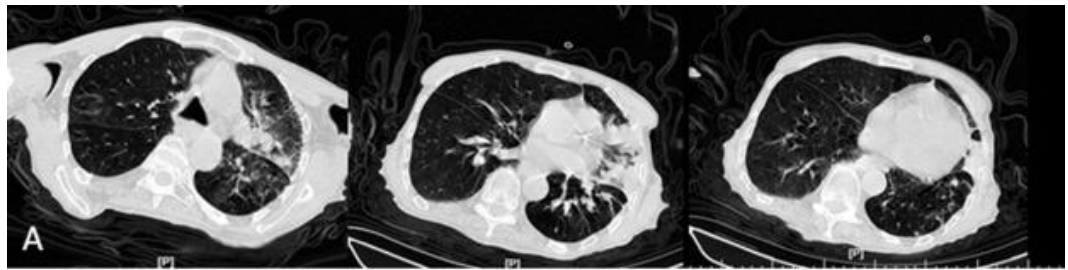
and systemic lupus erythematosus (SLE)

Anticoagulation prior to onset of intracranial hemorrhage

- Data on anticoagulation in COVID-19 patients prior to onset of ICH was reported in 8 ($n = 114$ patients)
- . Overall, 58 patients (50.9%) were on some form of anticoagulation.
- The indication for anticoagulation was part of in-hospital treatment for COVID-19 (standard prophylaxis elevated D-dimers and extracorporeal membrane oxygenation (ECMO) in majority of these patients (84%).
- The rest were on therapeutic anticoagulation for non-COVID-19 indications
- **Mortality in COVID-19 patients with intracranial hemorrhage**
- Across the 14 studies ($n = 111$ patients) (Table that reported data on mortality in COVID-19 patients with ICH, the mortality rate was 48.6%.

- **role** of the severe acute respiratory syndrome 2 (SARS-CoV-2) virus in the development of ICH in COVID-19 patients is **still unclear**. Majority of these patients had classic **Framingham risk factors** such as advanced age,
- being male,
- and pre-existing illnesses such as hypertension and diabetes mellitus, which are well-established risk factors for vascular degenerative changes, that could have predisposed them to the development of ICH

- Further, a significant proportion of patients were on some form of anticoagulation therapy, which could have predisposed them to the development of ICH. This is consistent with a recent retrospective study of 3824 COVID-19 patients by Melmed and colleagues in which **anticoagulation was associated with a 5-fold increase** in the risk of ICH.
- The association between anticoagulation and risk of ICH in COVID-19 patients was **confirmed**. Some of the patients however had no prior illnesses or risk factors that could explain the ICH leading to speculations about possible causal role of the SARS-CoV-2 virus.



COVID19 infection and concomitant aneurysmal

- 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-1 β and TNF α (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.

COVID-19-associated spontaneous subacute subdural haematoma: report of two cases

- Several kinds of coronavirus-associated disorders, including vascular involvements with [neurological symptoms](#), have been reported worldwide. Here, we describe two individuals with COVID-19 with no history of traumatic brain injury nor of vascular injuries, who developed spontaneous [subdural haematoma](#) in a subacute process. Both individuals became lethargic and unresponsive during admission in the intensive care unit. Both have undergone emergent [craniotomy](#) with acceptable outcome

- **Spinal epidural abscess in COVID-19 patients**

- **COVID-19 tsunami: the first case of a spinal cord injury patient in Italy**
- **Case presentation**
- A 56-year-old male with AIS A C4 tetraplegia developed fever during the night, without any prodrome