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Clinical research

Intracerebral hemorrhage associated COVID-19 patient with normal coagulation profile after ECMO treatment: A case report

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A B S T R A C T

Objective: Coronavirus disease 2019 (COVID-19) is a novel coronavirus-caused infectious acute respiratory disease that can progress to severe acute respiratory distress syndrome (ARDS). For severe cases, extracorporeal membrane oxygenation (ECMO) is an excellent treatment option. ECMO had a number of side effects, including bleeding. Intracerebral hemorrhage can occur in COVID patients due to a variety of mechanisms, including covid’s effect on ACE-2 receptors and subsequent hypertension, coagulopathy, DIC, or medication, such as anticoagulant use.

Case presentation: We present a case of a 53-year-old male COVID-19 patient who developed multiple, massive, severe intracerebral hemorrhages (ICH) despite a normal coagulation profile after ECMO treatment.

Conclusion: COVID-19 can progress to severe acute respiratory distress syndrome (ARDS), necessitating the use of extracorporeal membrane oxygenation (ECMO). Although ICH is not a common complication in patients with COVID-19 disease, it is unknown why this patient had a lower threshold of ICH despite having a normal coagulation profile.

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gression over the admission days. The swab was tested for COVID-19 infection using RT-PCR. Furthermore, even with an optimal coagulation profile, the hemorrhage worsened over time, and no specific pattern was observed, as shown in Fig. 2 which showed images of the last CT brain which illustrated massive multiple ICH with increased ventricular compression, increased IVH, increased SAH and increased the inferior displacement of the cerebellar tonsils (herniation). During ECMO, the patient was ventilated as follows: pressure control (PC) with pressure support (PS), tidal volume (TV) was target 3–4 ml/kg, PEEP decreased 14 to 5 cmH2O, respiratory rate (RR) was 12/min, arterial blood gas (ABG) was partial pressure of oxygen (PO2) was 71.2, co2 was 44.3, and mixed venous saturation was 66 percent. Our national guidelines protocol for Covid 19 management includes antibiotics, antiviral Covid-19 treatment, vitamin replacement, steroids, and cytokine IL6 antagonist Tocilizumab IV two doses as protocol. With fixed acceptable coagulation profiles during case follow up as shown in Table 1, there was an improvement in chest X-ray and ABG. Bacterial growth was not detected in blood cultures. The echocardiogram was normal. The patient was continued on ECMO treatment and ICU supportive measures for eleven days, but unfortunately, he died because of severe COVID-19 infection and massive ICH.

3. Discussion

Coronavirus disease 2019 (COVID-19) is a new coronavirus-caused acute infectious respiratory disease.1 COVID-19 disease can progress to severe acute respiratory distress syndrome (ARDS) lead to consider extracorporeal membrane oxygenation (ECMO).2 ECMO appears effective to treat ARDS in many conditions include COVID-19.3,4 Bleeding is one of the most serious ECMO complications, but achieving a normal coagulation profile can help prevent it.5 Our patient’s coagulation profile was kept normal and optimal (no heparin infusions or boluses were given except for 10,000 units during cannulation). COVID-19 disease, on the other hand, appears to be a risk factor for coagulopathy,6 and to reduce the influence of precipitating events, Anticoagulation is typically achieved by a continuous intravenous infusion of unfractionated heparin (UFH) targeting an APTT of 60–80 s, as well as activated clotting time (ACT) with a treatment target of 180–220 s. Fluid-blood levels in acute intracerebral hemorrhage may indicate the presence of coagulopathy with moderate sensitivity and high specificity, according to CT findings.7 ICH is uncommon in COVID-19 patients and is associated with a high mortality rate.8 The pathophysiology of ICH in a COVID-19 patient is unknown; however, there was massive ICH in our case despite the use of therapeutic anticoagulation. This hemorrhage could be explained by hypoxia in Covid-19 patients, which causes disruption of the blood brain barrier and increased susceptibility to intracerebral hemorrhage, according to Rich et al.9 While Ding et al. demonstrated the neuroinvasive potential of corona virus in his study on corona-related types,10,11 Varga et al. and Ackermann et al. also found autopsy evidence of vasculitis in SARS-Cov-1. Endothelial damage occurs in SARS-Cov-2, and microscopic descriptions of endothelial cerebral veins may result in microscopic bleeds and eventual intracerebral hemorrhage.12–14 Multiple studies have drawn attention to the facilitated entry of COVID-19 in its host, which has been shown to be via the Angiotension Converting Enzyme 2 (ACE2) receptors of the Human cell surface mediated by its S-Protein, patients with hypertension have reduced ACE2 expression in patients with
Covid-19 virus occupied this receptors with furthermore reduction of ACE2 with subsequent increase of the ICH with elevated blood pressure.\textsuperscript{1,2} Another hypothesis proposed Covid-19 patients frequently have prolonged prothrombin time and coagulopathy, which increases the risk of secondary intracerebral haemorrhage.\textsuperscript{3} Furthermore, Covid-19 infection causes distinct coagulopathy in the form of increased D-dimer concentration, prolonged prothrombin time, platelet dysfunction, and DIC, as described by Ding et al. in their study of Corona virus-related types.\textsuperscript{4} Other studies support that COVID-19 patients with severe illness are also at risk for ICH.\textsuperscript{5,6} According to some studies, the use of anticoagulants is associated with an increased risk of ICH in the future.\textsuperscript{7} Hence, we described a COVID-19 patient who developed multiple massive ICH hemorrhages despite receiving a low prophylactic dose of low molecular weight heparin and having a normal optimal coagulation profile. The hemorrhage worsened over time even with an optimal coagulation profile, as shown in Fig. 1. We supposed that the cause of this ICH is due to both the COVID-19 infection severity and also the ECMO treatment usage with co-existence risk variables. Those variables includes the ECMO duration, usage of antithrombotic therapy, altered intrinsic coagulation, renal function status, blood components’ need, rapid hypercapnia at ECMO initiation, and even pre-ECMO morbidity.\textsuperscript{8} Our findings highlight the importance of further research into coagulation abnormalities in Covid-19 patients in order to assess the risk of hemorrhagic complications as a result of COVID-19 disease.

### Conclusion

COVID-19 can progress to severe acute respiratory distress syndrome (ARDS), necessitating the use of extracorporeal membrane oxygenation (ECMO). Although ICH is not a common complication in patients with COVID-19 disease, it is unknown why this patient had a lower threshold of ICH despite having a normal coagulation profile.

Compliance with ethical standards.

### Ethics approval and consent to participate

The study was approved by the Ethics Committee of King Salman Armed Forces Hospital (KSAFH) on December 5th 2020 (KSAFH-REC-2020-376). Written informed consent was obtained from the patient.

### Declaration of competing interest

All authors declare that they have no conflicts of interest. All the authors have consented to the publication of this manuscript.

### Data access statement

All manuscript data are available and included in the study and already there is an ethical approval. If furthers documents or images needed we will provide it.

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### Table 1

| Day/ Coagulation screening | PT (11–13.5 sec.) | APTT (60–80 sec.) | INR (0.8–1.2) | ACT (70–120 sec.) |
|---------------------------|-------------------|------------------|--------------|------------------|
| Day 1                     | 21.30             | 81.10            | 1.60         | 215              |
| Day 2                     | 20.10             | 33.10            | 1.51         | 173              |
| Day 3                     | 20.80             | 28.50            | 1.56         | 225              |
| Day 4                     | 25.80             | 42.10            | 1.92         | 228              |
| Day 5                     | 21.60             | 36.40            | 1.62         | 164              |
| Day 6                     | 19.90             | 33.30            | 1.50         | 232              |
| Day 7                     | 19.50             | 32.10            | 1.47         | 179              |
| Day 8                     | 18.80             | 32.10            | 1.42         | 135              |
| Day 9                     | 17.60             | 29.30            | 1.33         | 172              |
| Day 10                    | 17.50             | 34.80            | 1.33         | 126              |
| Day 11                    | 17.10             | 36.80            | 1.30         | 137              |
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