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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Case Reports & Case Series

Intracranial hemorrhage in a young COVID-19 patient

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ABSTRACT

COVID-19 patients are increasingly understood to develop multisystem manifestations, including neurologic involvement. We report the case of a 42-year old COVID-19 positive patient with a fatal intracerebral hemorrhage (ICH). The patient presented with fever and dyspnea, requiring intubation due to medical complications. After prolonged sedation and anticoagulation, the patient suddenly developed bilaterally fixed and dilated pupils, caused by a right-sided intracranial hemorrhage with uncal herniation. The course of this case illustrates the delicate balance between hypercoagulability and coagulation factor depletion; especially in the intubated and sedated patient, in whom regular neurological assessments are impeded. As we expand our understanding of the neurological ramifications of COVID-19, clinicians need to be increasingly aware of the precarious coagulation balance.

1. Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) continues to pose significant challenges to healthcare systems and the global community. SARS-CoV-2 has been associated with a variety of multi-organ complications, with an increasing proportion of patients presenting with extrapulmonary symptoms [1]. COVID-19 has been linked to thrombosis and stroke [2,3]. However, significant hemorrhage has also been observed, possibly indicating depletion of the coagulation system [4,5]. We report the case of a patient with COVID-19 and a complex clinical course leading to an intracerebral hemorrhage with rapid neurological deterioration and fatal outcome.

2. Case presentation

A 42-year-old man, who had immigrated from Nepal to the United States in 2017, presented to the emergency department on March 29th, 2020 with a severe cough after being diagnosed with COVID-19 at an outpatient clinic five days prior. His past medical history included hypertension and gastritis. He reported having a cough for a month prior to presentation and fevers for the past week. In the emergency department, the patient was febrile, (103°F), tachycardic (103 bpm), and tachypneic (23 bpm) with dyspnea and pleuritic chest pain. Chest radiography showed bilateral opacities consistent with multifocal pneumonia. He was given one dose of cefazolin and was placed on daily azithromycin. Initial laboratory workup showed elevated levels of ferritin (409 ng/mL), lactate dehydrogenase (355 u/L), and elevated C-reactive protein (31·1 mg/L). Platelets (127,000/μL), prothrombin time (9·8 s), partial thromboplastin time (23·5s), and D-dimer (< 0·19 μgFEU/mL) levels were all within normal limits.

The patient was admitted to the COVID-19 medical intensive care unit, his respiratory status rapidly deteriorated; he was intubated within 30 h of admission and diagnosed with acute respiratory distress syndrome. The patient was started on steroids and placed in the prone position for 16 h a day. Interleukin-6 level was elevated (178 pg/mL), and immunosuppressive therapy with tocilizumab was initiated with no immediate response. On hospital-day 16, his D-dimer levels continued to be elevated (5·11 μgFEU/mL) (Fig. 2), and the patient was placed on a heparin drip. with an aPTT goal of 55·6-66·4 s. One day later, the patient developed non-oliguric acute renal failure and was started on continuous replacement renal therapy for the management of hypervolemia and hyperkalemia. Routine neurological examinations every four hours were stable until hospital-day 24, when unilateral pupillary changes rapidly progressed to bilaterally fixed and dilated

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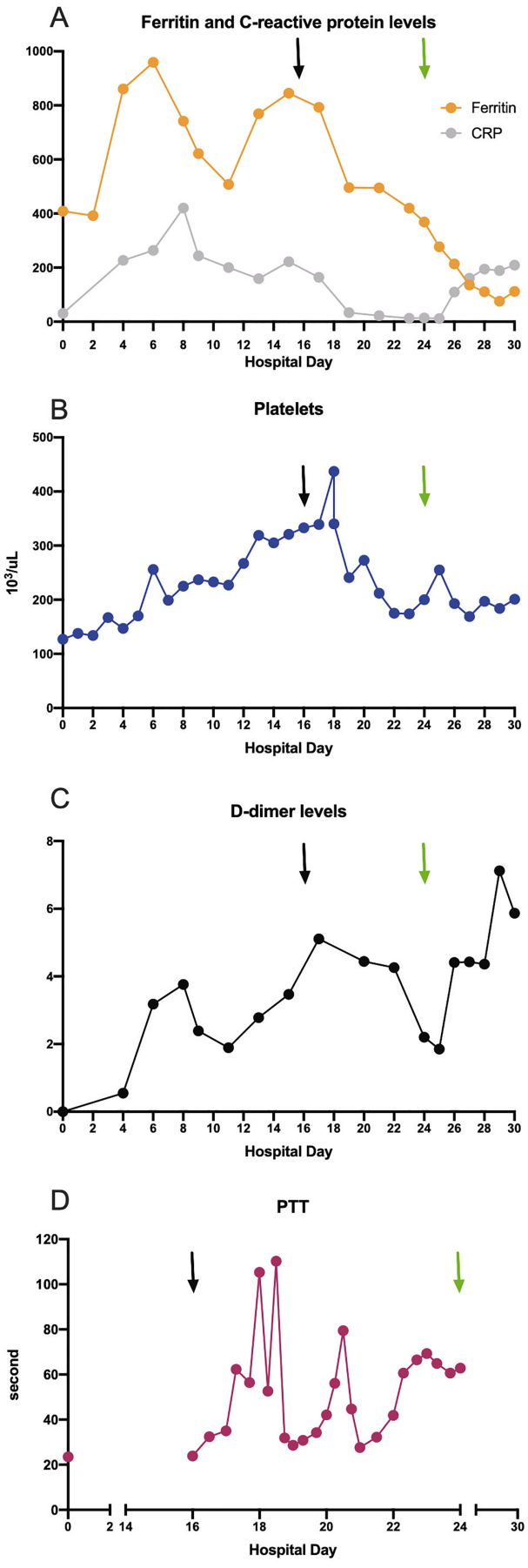

Fig. 1. Axial computed tomography of the brain showing a large, multiloculated right-sided intracerebral hemorrhage centered in the lentiform nucleus with associated uncal herniation and severe sub-falcine herniation.

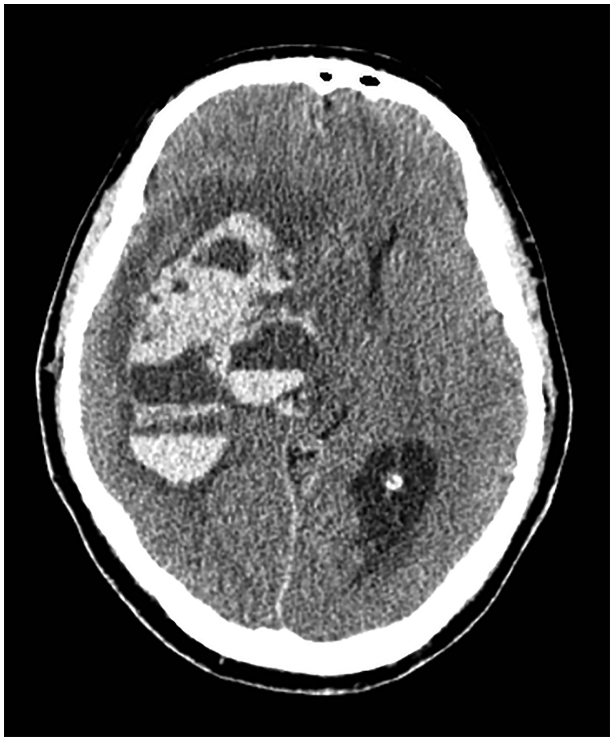

Fig. 2. Graphical representations of laboratory marker values across the hospital admission. The respective levels are shown for C-reactive protein and ferritin (A), platelet counts (B), D-dimer (C), and PTT levels (D). The black arrow denotes the initiation of intravenous heparin therapy. The green arrow denotes the time of detection of pupillary anisocoria.

pupils. Computed tomography of the head demonstrated a large, multiloculated right sided intracerebral hemorrhage associated with vasogenic edema, as well as uncal and sub-falcine herniation with no evidence of an underlying ischemic stroke (Fig. 1). Vital signs were within normal range prior to and for the first several hours of pupillary anisocoria. The patient subsequently lost all brain stem reflexes over four hours but continued to breathe over the ventilator precluding brain death testing for seven days until the patient's family elected to pursue comfort measures and withdrawal of care on hospital-day 32.

3. Discussion

An increasing number of reports describe COVID-19 related hypercoagulation, recommending more aggressive hydration and anticoagulation in COVID-19 positive patients. These measures increase the risk of hemorrhage, especially with the potentially brittle coagulation physiology exhibited by COVID-19 patients. It is also possible that this patient suffered a hemorrhagic conversion of an acute or subacute infarct. Stroke is an established potential complication associated with COVID-19.[13] Therefore, in the setting of heparinization, it is possible that a hemorrhagic transformation occurred. This would be consistent with the multiloculated appearance of the bleed.

Extreme supraphysiologic ventilator settings in intubated and sedated COVID-19 patients prevent sedation pauses, thereby precluding comprehensive neurological assessments. Various physiological tools can augment the neurological examination while maintaining adequate sedation including frequent pupillometer checks, bi-spectral index, electroencephalography, evoked potentials, transcranial dopplers, and

near-infrared spectroscopy. Once the patient's medical status allows for safe neurological examinations, we strongly encourage it. Biomarkers can guide therapy but have not been well identified in COVID-19 patients. Elevated ferritin levels in Covid-19 patients have been associated with higher incidence of stroke, while very high ferritin levels on admission, as seen in this case, correlated with a high mortality rate in COVID-19 patients [3,6]. IL-6, described as a biomarker for in-hospital mortality, was also elevated in this patient [7]. Of note, patients immigrating from areas at high altitude, such as Nepal, have shown predisposition for thrombotic coagulopathies and may be at a higher risk in COVID-related coagulopathies [8].

4. Conclusion

CNS involvement has been more readily associated with COVID-19 patients, thereby compounding the morbidity and mortality of this critically ill patient population. Clinicians need to be aware of this correlation and carefully monitor patient's neurological status as part of their routine care.

Disclosures

All authors have no disclosures.

CRediT authorship contribution statement

Nicolas K. Khattar: Data curation, Writing - original draft, Visualization, Investigation. **Mayur Sharma:** Writing - original draft. **Abigail P. McCallum:** Methodology. **Brent G. Oxford:** Methodology. **Hassan Zeb:** Methodology, Software. **Sally A. Suliman:** Methodology, Supervision. **Emily P. Sieg:** Supervision. **J Mocco:** Writing - review & editing. **Joseph S. Neimat:** Writing - review & editing, Supervision. **Ajmal Zemmar:** Writing - review & editing, Supervision.

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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