Cerebral venous thrombosis in patients with severe COVID-19 infection in intensive care

K Keaney[1]

T Mumtaz[1]

Author details can be found at the end of this article

Correspondence to:
K Keaney;
katherine.keaney@nhs.net

Introduction

The novel coronavirus (SARS-CoV-2) was first isolated in the Hubei Province of China in early 2020. The respiratory virus spread rapidly leading to the current global pandemic. At the time of writing, the number of confirmed cases worldwide has reached almost 4 million (World Health Organization, 2020).

In patients with COVID-19 infection, a higher than expected incidence of thrombotic complications has been observed. One study reports a 31% incidence of thrombotic complications including pulmonary embolism, ischaemic stroke and myocardial infarction

Case report 1

A 51-year-old man with no comorbidities presented to hospital with a history of 3 days of fever, cough and shortness of breath, consistent with SARS-CoV-2 pneumonia. Computed tomography pulmonary angiogram on arrival showed extensive ground-glass opacification with dense consolidation throughout both lower lobes, but no central pulmonary embolus. D-dimer levels were normal.

He was admitted to a medical ward for continuous positive airway pressure but was transferred on day 3 to intensive care for invasive ventilation and further management. During his intensive care unit stay, he developed myocarditis and acute kidney injury. Dual antiplatelet therapy was commenced following cardiology input and he was therapeutically anticoagulated for haemofiltration.

His cardiorespiratory function gradually improved and sedative medications were stopped from day 11 to facilitate extubation. At day 15 he remained unresponsive and was noted to have bilateral dilated pupils with slow response to light. The patient became haemodynamically unstable overnight with progressively worsening hypotension and hypercapnia, with subsequent fixed and dilated pupils. Computed tomography of the head was carried out on day 16 (Figure 1). This showed superior sagittal sinus thrombosis with haemorrhagic venous infarction within the right frontal and parietal lobes, midline shift of 1 cm and cerebellar tonsillar herniation. This represented irreversible neurological dysfunction and he subsequently failed brainstem testing. The patient died later that day.

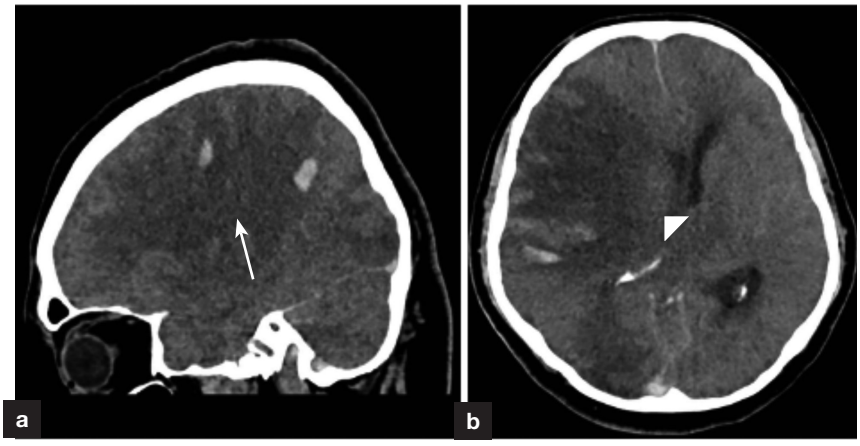

Figure 1. a. Contrast-enhanced axial and (b) sagittal computed tomography images of the brain demonstrating a filling defect within the superior sagittal sinus from the posterior parietal region to the level of the torcula herophilli, in keeping with a superior sagittal sinus thrombus. There is resultant haemorrhagic venous infarction (arrow) within the right frontal and parietal lobes. Note midline shift of 1 cm (arrow head) and cerebellar tonsillar herniation.

How to cite this article:
Keaney K, Mumtaz T. Cerebral venous thrombosis in patients with severe COVID-19 infection in intensive care. Br J Hosp Med. 2020. https://doi.org/10.12968/hmed.2020.0327

Case report 2

A 72-year-old woman with a past medical history of hypertension, type 2 diabetes mellitus and mild asthma presented with shortness of breath, hypoxia and lymphopenia. A chest X-ray showed radiological features of COVID-19 infection. She was managed for 3 days on a medical ward with 60% oxygen via Venturi mask then escalated to continuous positive airway pressure following a failed discharge. She was transferred to intensive care 12 days after initial presentation as a result of increasing dyspnoea and hypoxia, requiring urgent intubation and ventilation. Her oxygenation subsequently improved so computed tomography pulmonary angiogram was not carried out.

The patient was managed with a course of intravenous antibiotics as a result of suspected secondary infection, plus prophylactic enoxaparin as per policy. Sedation was weaned off on day 11 and she was successfully extubated onto continuous positive airway pressure. She subsequently developed progressive agitation and dyspnoea, requiring reintubation on day 13. Anticoagulation was escalated to treatment dose low molecular weight heparin to treat a potential pulmonary thrombus. On day 15, her pupils were noted to be dilated bilaterally and unresponsive to light, so an urgent computed tomography scan of the head was done (Figure 2). This showed extensive haemorrhagic infarct encompassing the right anterior cerebral, middle cerebral and posterior communicating artery territories with significant cerebral oedema and subfalcine, subtentorial and cerebellar tonsillar herniation. Superior sagittal sinus thrombosis was reported as the likely cause. This was discussed with the on-call neurosurgeons who confirmed this was unsalvageable and advised best supportive care. Her family were called and treatment ws withdrawn that evening.

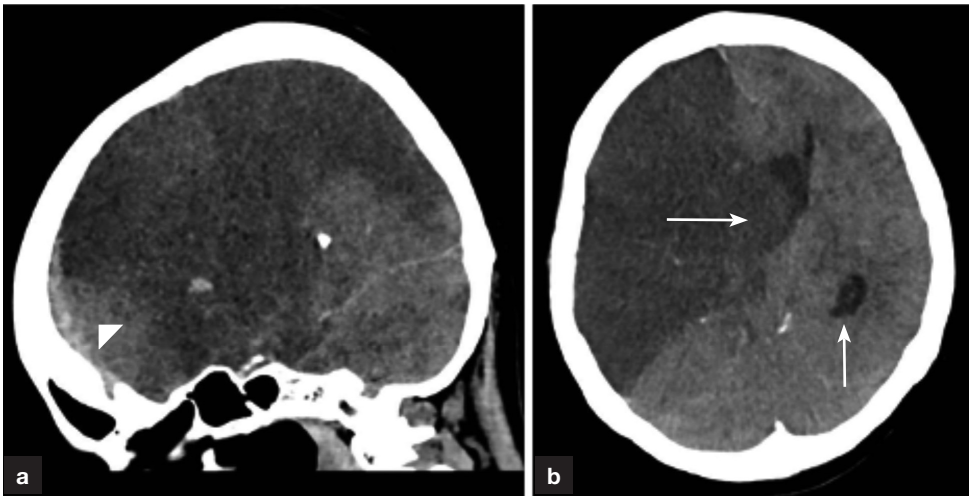

Figure 2. a. Contrast-enhanced axial and (b) sagittal computed tomography images of the brain. Findings are in keeping with a haemorrhagic infarct which encompasses the right anterior cerebral, middle cerebral and posterior communicating artery territories with significant cerebral oedema and resultant subfalcine, subtentorial and cerebellar tonsillar herniation. There is a midline shift of 2 cm towards the left (horizontal arrow in b), and further ischaemic infarct involving the watershed area of the left posterior communicating and middle cerebral artery territory (vertical arrow in b). Heterogeneous hypodensity involving the superior sagittal sinus can be seen, which is highly suggestive of superior sagittal sinus thrombus (arrow head in a).

in a cohort of intensive care unit patients, despite thromboprophylaxis (Klok et al, 2020). A similar incidence of thrombosis has been observed in the authors' local hospitalised patients during this pandemic.

A study using duplex ultrasound in intensive care unit patients reported an incidence of peripheral venous thromboembolism as high as 69%, and confirmed pulmonary embolism in 23% (Llitjos et al, 2020). Another study assessed coagulation profiles in a small group of patients on admission to intensive care with acute respiratory distress syndrome secondary to COVID-19. The results showed severe hypercoagulability with markedly raised fibrinogen levels and excessive fibrin polymerisation compared to healthy controls. This may contribute to direct pulmonary damage by fibrin deposition, while promoting systemic microvascular and venous thromboembolic complications (Spiezia et al, 2020).

Learning points

- Patients with COVID-19 are at increased risk of thrombotic complications.
- An increased dose of thromboprophylactic medications should be considered in patients with COVID-19 who require intensive care.
- Monitoring of anti-factor Xa may be useful to achieve a therapeutic dose of anticoagulant.
- Diagnosis of cerebral thrombosis may be delayed or missed in patients requiring mechanical ventilation and sedation.

Cerebrovascular infarction is being reported as a complication of COVID-19 but the overall incidence is currently unknown. Cerebral venous thrombosis is relatively rare, with around 13–15 cases per million per year (Devasagayam et al, 2016), comprising 0.5–1% of all strokes. Mortality varies between studies but is generally reported as up to 38% (Soyer et al, 2016). This case report highlights central venous sinus thrombosis as an important thromboembolic complication of severe COVID-19 infection in intensive care patients.

Discussion

While the aetiology of hypercoagulability in severe COVID-19 is not yet fully understood, it is becoming clear that these patients are at increased risk of thromboembolic events such as pulmonary thrombosis, venous thromboembolism and ischaemic stroke, despite being given anticoagulation. The suggested pathophysiological mechanism appears to be in situ thrombus formation as a result of the inflammatory response and prolonged immobilisation.

In the above cases, both patients were maintained on sedative medications for more than 10 days and neurological signs were only recognisable following the withdrawal of sedation. Patients with COVID-19 presenting to intensive care require prolonged mechanical ventilation and sedation, therefore the diagnosis of intracranial infarction may easily be missed or delayed.

Conclusions

This pair of cases of cerebral venous sinus thrombosis in intensive care unit patients with COVID-19 represents a possibly under-reported complication of severe infection. Since these cases, local policy was amended to increase the thromboprophylaxis dose, lower the threshold for diagnostic imaging to identify thrombi and commence therapeutic anticoagulation earlier in the disease process. Additionally, empirical (weight-based) dosing of anticoagulants may be insufficient in preventing thrombosis in this population. Following advice from the local haematology team, anti-factor Xa blood levels were taken from patients with COVID-19 and the relative dose of low molecular weight heparin was titrated to achieve a therapeutic target range. This ensured each patient received a full therapeutic dose of anticoagulant. In addition, patients with COVID-19 who had been discharged received an extended period of thromboprophylaxis.

More research into the aetiology and clinical implications of hypercoagulability in these patients is required to develop an evidence-based protocol for early anticoagulation, diagnosis and treatment of thrombotic complications.

Author details

[1]Intensive Care Department, Barnet Hospital, Hertfordshire

References

Devasagayam S, Wyatt B, Leyden J et al. Cerebral venous sinus thrombosis incidence is higher than previously thought. Stroke. 2016;47(9):2180–2182. https://doi.org/10.1161/STROKEAHA.116.013617

Klok FA, Kruip MJHA, van der Meer NJM et al. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. Thromb Res. 2020;191:145–147. https://doi.org/10.1016/j.thromres.2020.04.013

Llitjos J-F, Leclerc M, Chochois C et al. High incidence of venous thromboembolic events in anticoagulated severe COVID-19 patients. J Thromb Haemost. 2020;18(7):1743–1746. https://doi.org/10.1111/jth.14869

Soyer B, Rusca M, Lukaszewicz A-C et al. Outcome of a cohort of severe cerebral venous sinus thrombosis in intensive care. Ann Intensive Care. 2016;6(1):29. https://doi.org/10.1186/s13613-016-0135-7

Spiezia L, Boscolo A, Poletto F et al. Coagulation profiles in COVID-19 patients. Thromb Haemost. 2020;120(06):998–1000. https://doi.org/10.1055/s-0040-1710018

World Health Organization. Coronavirus disease (COVID-19) Situation report-111. 2020. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200510covid-19-sitrep-111.pdf?sfvrsn=1896976f_2#:~:text=Situation%20Report%20%E2%80%93%20111%20Data%20as%20received%20by,the%20current%20evidence%20on%20the%20impact%20of%20angiotensin-(accessed 7 September 2020)