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Cerebral venous sinus thrombosis associated with COVID-19

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Abstract

Coronavirus disease of 2019 (COVID-19) is well known to increase the risk of developing venous thromboembolism and so may present first to neurologists owing to development of cerebral venous sinus thrombosis. We present a patient presenting acutely with delirium, who after initial negative viral testing, was diagnosed with cerebral venous sinus thrombosis in association with COVID-19.

Case report

A 50-year-old man presented with delirium. PCR nasopharyngeal swabs for the severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) were negative but we made a diagnosis of probable COVID-19 based on clinical and radiological features according to European Centre for Disease Control case definition criteria.¹ Fibrinogen was 3.8 g/L (1.8–5.4) and neutrophil:lymphocyte ratio 14.4; age \geq 50 years and neutrophil:lymphocyte ratio \geq 3.13 have been associated with severe disease.² D-dimer was not recorded acutely. A non-contrasted CT scan of head and CSF analysis on admission were normal. We started enoxaparin 40mg once daily subcutaneously as prophylaxis for venous thromboembolism and he did not need ventilator support.

Despite clinical improvement, he had persisting problems with executive dysfunction and dyspraxia. Repeat CT scan of head and CT venogram one week following admission showed dural venous sinus thrombosis involving the whole of the superior sagittal sinus, left transverse sinus and left sigmoid

sinus down to the level of the jugular foramen. The vein of Labbé was also thrombosed and there was a small (7 x 8 mm) parenchymal haemorrhage within the left temporal lobe (figure 1). Shallow CSF density subdural collections were consistent with small hygromas (maximum depth 8 mm). The radiological findings were in keeping with his cognitive profile although we noted that he did not have dysphasia. We fully anticoagulated him with intravenous heparin. After a further week, there was clinical and radiological improvement with re-canalisation of the vein of Labbé, partial re-canalisation of the left transverse sinus and superior sagittal sinus, reduced oedema in the left temporal lobe, but some acute haemorrhage within the slender hygromas. We briefly treated him with enoxaparin 1.5 mg/kg daily before switching to a direct oral anticoagulant on discharge from hospital. His anti-cardiolipin antibodies returned a positive result (278 IgG Phospholipid Units) but were not detected on interval testing (12 weeks). Beta-2 glycoprotein 1 IgM and IgG were normal.

Discussion

Several studies have reported significantly increased rates of venous and arterial thromboses in patients with COVID-19 despite administration of standard prophylaxis, particularly amongst those with severe disease requiring intensive care support.³⁻⁵ The presence of venous thromboembolism has been associated with an increased risk of death.^{4,5} Our centre noted 13 imaging-confirmed thromboembolic events in 12 of a total 352 (3.4%) consecutive patients requiring hospital admission for confirmed COVID-19 (9th March 2020 to 26th April 2020). This compares with a reported incidence of 2% in H1N1 influenza.⁶ To date however, cerebral venous sinus thrombosis has only rarely been reported in the context of COVID-19.^{7,8}

The mechanism responsible for increased risk of thrombosis in COVID-19 is now beginning to be understood.^{9,10} Angiotensin-converting enzyme 2 receptor facilitates cell entry of SARS-CoV-2,¹¹ and is expressed on endothelial cells in multiple organ systems.¹² Viral infection of endothelial cells with associated endotheliitis¹³ and histological evidence of complement-mediated thrombotic microvascular injury have been demonstrated in COVID-19.¹⁴ Together with cytokine abnormalities,¹⁰ these contribute to vasoconstriction, ischaemia, inflammation, and hyper-coagulopathy. Anti-phospholipid antibodies are common in severely ill patients and have previously been reported in the context of COVID-19. Their contribution to the development of coagulopathy remains uncertain and, as in this case, they may be transient.¹⁵ However, it has also been suggested that anti-cardiolipin antibodies may identify patients at greater risk of cerebral infarction.¹⁶

The optimal choice of anticoagulant and duration of treatment for cerebral venous sinus thrombosis are not known,¹⁷ and there are additional uncertainties in the thrombosis associated with COVID-19.¹⁸ We elected to use a direct oral anticoagulant before the anti-cardiolipin antibody result becoming available on the basis of ease of administration. Direct oral anticoagulants may be less effective than warfarin in the context of anti-phospholipid syndrome,¹⁹ although there is evidence to support their use in low risk i.e. not 'triple positive' (anti-cardiolipin antibody, anti-glycoprotein 1 antibody and lupus anticoagulant) patients with anti-phospholipid syndrome and prior venous thromboembolism.²⁰ This patient has shown a positive response to treatment to date and we anticipate continuing anticoagulation for a minimum of 3 months,²¹ but will continue to review treatment.

This report highlights both the need to consider cerebral venous sinus thrombosis in patients presenting with headache, encephalopathy or focal neurological deficits.

Key Points

- COVID-19 is commonly associated with coagulopathy

- Cerebral venous sinus thrombosis associated with COVID-19 may present acutely to neurologists
- The optimal choice of anticoagulant and duration of treatment for cerebral venous sinus thrombosis in the context of COVID-19 remains uncertain

Competing interests

The authors have no competing interests to declare.

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Contributorship

All authors contributed to data collection and analysis as well as drafting and review of the manuscript

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Figure legend

Figure 1 Cerebral venous sinus thrombosis with haemorrhagic infarct associated with COVID-19

A CT scan of head with contrast (1mm axial) showing left transverse sinus thrombosis

B CT scan of head with contrast (sagittal) showing extensive superior sagittal sinus thrombosis

C CT scan of head (2mm coronal minimum intensity projection) showing haemorrhagic infarct and surrounding oedema in the left temporal lobe