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Case Report

CASE REPORT

Large-vessel thrombotic stroke despite concurrent therapeutic anticoagulation in COVID-19-positive patient

Andrew Shoukry[1,*,†] and Thomas A. Kite[2]

[1]Trent Cardiac Centre, Nottingham University Hospitals NHS Trust, Nottingham, UK, [2]Trent Cardiac Centre, Nottingham University Hospitals NHS Trust, Nottingham, UK

*Correspondence address. Andrew Shoukry. Tel: +0115 969 1169; E-mail: Andrew.shoukry@nhs.net

Abstract

The current COVID-19 pandemic caused by the novel SARS-CoV-2 virus is now recognized to be associated with a coagulopathy that can result in arterial and venous thromboses. In this report, we describe a case of large-vessel cerebrovascular thrombus in a therapeutically anticoagulated 89-year-old male admitted with COVID-19 infection. Despite clinical improvement following COVID-19 pneumonitis, symptoms of an acute left-sided total anterior circulation stroke rapidly developed 10 days after initial COVID-19 symptom onset. Computed tomography angiography imaging confirmed acute large-vessel thrombus in the terminal segment of the internal carotid artery resulting in acute right middle cerebral artery territory infarction. Thromboembolic events in the context of COVID-19 infection have recently been described in critically unwell patients. However, to the best of our knowledge, this is one of the first cases of large-vessel thrombus in a patient with COVID-19 infection receiving concurrent therapeutic anticoagulation.

INTRODUCTION

A hypercoagulable state and propensity for thromboembolic disease have been increasingly described in recent reports of patients with COVID-19 infection, yet the exact mechanism driving this remains unclear. Recent discussions in the medical community have focused on the importance of prophylactic anticoagulation where appropriate to reduce the risk of thromboembolic events. This report highlights the case of a hospitalized patient diagnosed with COVID-19 infection who suffered a large-vessel acute thromboembolic stroke despite concurrent therapeutic anticoagulation. It suggests that in those who experience a profound systemic inflammatory response to the SARS-CoV-2 virus, there may be an increased risk of prothrombotic events, which may not be entirely attenuated by anticoagulation therapy.

CASE REPORT

An 89-year-old male presented with a 5-day history of worsening dyspnoea and cough. Past history included hypertension, ischaemic heart disease, permanent pacemaker implantation for complete heart block, chronic kidney disease stage 3 and atrial fibrillation. He was taking long-term Rivaroxaban therapy for stroke and systemic embolism prophylaxis. No compliance issues were reported. No antiplatelet or additional antithrombotic medication was being taken prior to hospital admission. Despite advanced age, the gentleman was fully independent with activities of daily living. Hospital admission was required due to hypoxia. Maximal oxygen requirements during the course of admission were 4 l/min. Reverse transcriptase viral polymerase chain reaction testing subsequently confirmed COVID-19 infection.

[†]Andrew Shoukry, http://orcid.org/0000-0002-0012-8288

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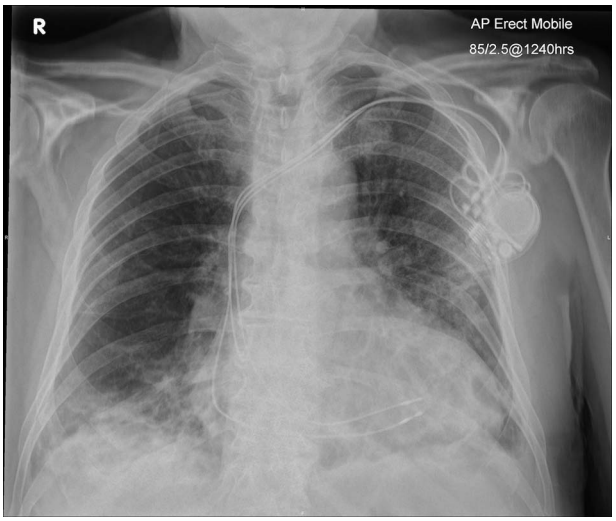

Figure 1: Chest radiography demonstrating bi-basal and peripheral left mid zone pulmonary infiltrates and previous left-sided dual chamber permanent pacemaker (with capped and buried right ventricular lead).

Admission blood testing demonstrated lymphopenia (0.82 × 10^9/l) and a markedly elevated C-reactive protein of 345 mg/l. Coagulation studies were prolonged (activated partial thromboplastin time 31.7 s, prothrombin time 14.4 s) due to concurrent anticoagulation with Rivaroxaban. Fibrinogen level was markedly elevated at 9 g/l. Creatinine (106 µmol/l) and estimated glomerular filtration rate (52 ml/min) were at the patient's baseline level. Remaining biochemistry results returned within normal limits. Chest radiography confirmed new bi-basal and peripheral left mid zone pulmonary infiltrates suggestive of COVID-19 pneumonitis (Fig. 1). Oral doxycycline was commenced to cover for possible secondary superadded bacterial infection, in line with local institutional protocols during the early period of the COVID-19 pandemic.

On Day 4 of his hospital stay, and despite an improvement in COVID-19 symptoms with reducing oxygen requirements, the patient developed a rapid and dense left-sided hemiplegia with dysarthria, alongside clinical signs of left gaze palsy and left homonymous hemianopia. National Institutes of Health Stroke Scale was 21, signifying symptoms suggestive of acute severe stroke. Within 1 h of onset of neurological symptoms (Day 4 of hospital admission), computed tomography imaging of the brain was performed. This showed a region of low attenuation in the right basal ganglia and high density in the right M1 segment of the middle cerebral artery consistent with an acute infarct due to large-vessel occlusion (Fig. 2). Computed tomography angiography was requested to evaluate a potential target for mechanical thrombectomy. This demonstrated extensive thrombus occluding the right cervical internal carotid artery and a T occlusion affecting the right anterior and middle cerebral arteries (Fig. 3).

The patient was not a candidate for thrombolytic therapy due to concurrent anticoagulation with Rivaroxaban. Mechanical thrombectomy was discussed with interventional radiology colleagues, but it was decided that this would offer little clinical benefit given the patient's age and comorbid status. Unfortunately, despite maximal ward-based medical treatment, the patient deteriorated and passed away 5 days later.

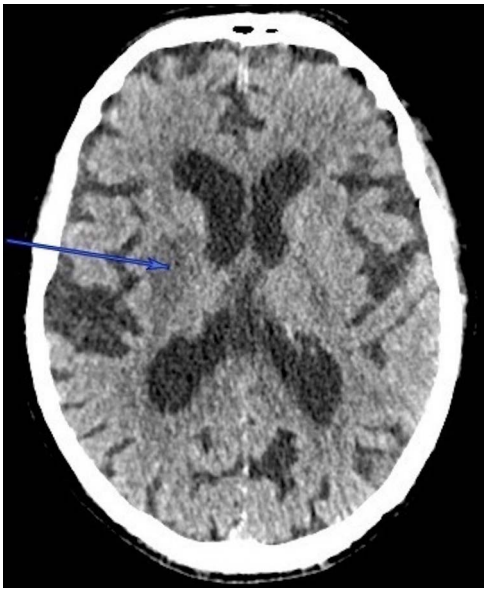

Figure 2: Computed tomography of the brain showing low attenuation in the right basal ganglia and high density in the right M1 segment of the middle cerebral artery.

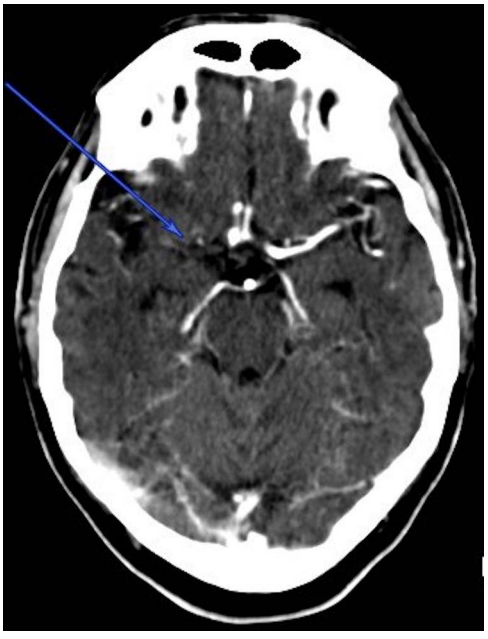

Figure 3: Computed tomography angiography demonstrating thrombus occluding the right middle cerebral artery.

DISCUSSION

This report describes a novel case of large-vessel thrombotic stroke in a recovering COVID-19-positive patient on therapeutic anticoagulation. Emerging evidence suggests the presence of a hypercoagulable state in patients with SARS-CoV-2 infection [1, 2], especially those hospitalized with severe illness and strong clinical risk factors for Venous thromboembolism (VTE) [3]. Recent case series has described large-vessel strokes in younger patients [4] and even thromboembolic complications in COVID-19 patients despite concurrent therapeutic anticoagulation [5]. The exact pathophysiology is currently unknown, but it is hypothesized that hypoxia, immobility, excessive secretion of proinflammatory cytokines and diffuse intravascular coagulation could all contribute to these clinically significant events [2]. Most have been observed in critically ill patients, with a recent observational study reporting 31% of 184

patients developing thromboembolic disease during intensive care unit stay [6].

Although this report cannot confirm a causal relationship between COVID-19 infection and large-vessel thrombotic stroke due to the presence of other competing vascular risk factors (hypertension, atrial fibrillation), it does offer further evidence that SARS-CoV-2 infection may increase the risk of thrombotic events such as stroke. Additionally, the timing of these events may be unpredictable and unrelated to peak COVID-19 disease severity. Given the acute cerebrovascular event occurred 9 days following symptom onset in this case (not accounting for pre-symptomatic phase of COVID-19), it could be speculated that thromboembolism may be more common in the second half of the COVID-19 disease course (Day 10 onwards), when a systemic inflammatory response reaction has been demonstrated to predominate [7]. In this case, the presence of both an elevated C-reactive protein and fibrinogen supports this assertion.

Nevertheless, despite this gentleman receiving concurrent therapeutic anticoagulation to reduce the risk of systemic thromboembolism, this does not appear to have sufficiently attenuated the increased thromboembolic risk posed by COVID-19 infection. Perhaps, there may be value in screening biochemistry and coagulation studies (possibly at point of admission) to risk stratify and identify those patients at highest risk for subsequent events. Elevated D-dimer levels have been shown to predict future mortality in COVID-19 [8], but a threshold for prediction of thromboembolism has yet be clearly defined. Fibrinogen levels could also be used as a method of prognostication to inform clinical management. Although there are no data in COVID-19 patients, previous studies have demonstrated that elevated fibrinogen levels are predictive of vascular events, including stroke [9].

Recent reports have proposed higher dose thromboprophylaxis therapy to be used in patients with COVID-19 infection [6, 10]. However, despite some institutions introducing these regimens into local protocols, there remains no randomized data to support a definitive conclusion and to suggest the superiority of one strategy versus another (low molecular weight heparin vs. Vitamin K antagonist vs. direct oral anticoagulant). A perceived protection against thromboembolism needs to be balanced against increased bleeding risk, including intracranial haemorrhage, in these patients. Randomized studies to establish the benefits, or not, of biomarker screening to predict the risk of thromboembolism, and varying anticoagulation strategies, are required to inform best clinical practice in the COVID-19 era.

ACKNOWLEDGEMENTS

Not applicable.

Conflict of interest statement. No conflict of interest.

FUNDING

Not applicable.

ETHICAL APPROVAL

No ethical approval required.

CONSENT

Written informed consent was obtained from the patient's next of kin and family for the publication of this case report and any accompanying images.

GUARANTOR

Andrew Shoukry and Thomas A. Kite.

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