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## “COVID-19 and cervical artery dissection- A causative association?”

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COVID-19 is a pandemic disease which predominantly affects the respiratory system, however it also causes multi-organ dysfunction in a subset of patients. There is a growing evidence that it increases the propensity of strokes in younger patients. Besides producing a prothrombotic state, arterial dissection could be one of its many manifestations, increasing the risks of stroke. Herein, we report the first case of spontaneous bilateral vertebral artery dissection in a patient with COVID-19. 39-year female presented with spontaneous bilateral vertebral artery dissections without any instigating traumatic events and no history of connective tissue disorders. Whether this patient's vertebral artery dissections were triggered by exaggerated inflammatory response or arteriopathy secondary to COVID-19 remains speculative. Nonetheless, arterial dissection could be one of its complications. It is important for the physicians to be aware of different clinical manifestations of COVID-19 as we manage these patients with no historical experience, to provide adequate care.

**Key Words:** Cervical dissection—COVID-19—Vertebral dissection—Stroke  
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### Introduction

Coronavirus disease 2019 (COVID-19) is a pandemic disease with serious public health risk. It has spread across the globe in a matter of few months. COVID-19 predominantly affects older at-risk population with comorbidities<sup>1</sup>; however, its widespread manifestations in all age-groups are increasingly being reported in the literature.<sup>1,2</sup> For the most part, respiratory system is affected, even so other organ systems are not spared either.<sup>1-3</sup>

There is a growing evidence that younger patients with no known risk factors are presenting with strokes, more commonly since this pandemic has started.<sup>4</sup> Although, the true relationship between COVID-19 and stroke incidence remains to be determined, there have been many reports in the literature indicating that COVID-19 may produce a prothrombotic state which can result in thromboembolic complications.<sup>5</sup> Coagulopathy and vascular endothelial dysfunction resulting from an exaggerated systemic inflammation or a “cytokine storm” have also been suggested as some of the many manifestations of Covid-19.<sup>6</sup> The endothelial dysfunction resulting from cytokine storm or direct SARS-CoV-2 invasion of the vascular endothelial cells using their surface angiotensin-converting enzyme 2 (ACE2) receptors<sup>7,8</sup> can potentially result in vascular dissection.

There are a couple of case reports in the literature describing the patients who presented with vascular dissection without any inciting factors.<sup>9,10</sup> Whether the increased propensity and the pathogenesis resulting in dissection is triggered by COVID-19 is largely unknown, it does require continued observation and further investigations.

Herein, we report the first case of spontaneous bilateral vertebral artery dissection in a patient with COVID-19

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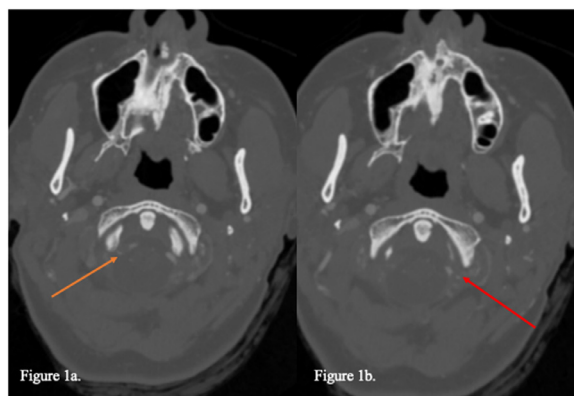
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infection. It is important for the physicians to be aware of different clinical manifestations of COVID-19 as we manage these patients with no historical experience, to provide adequate care.

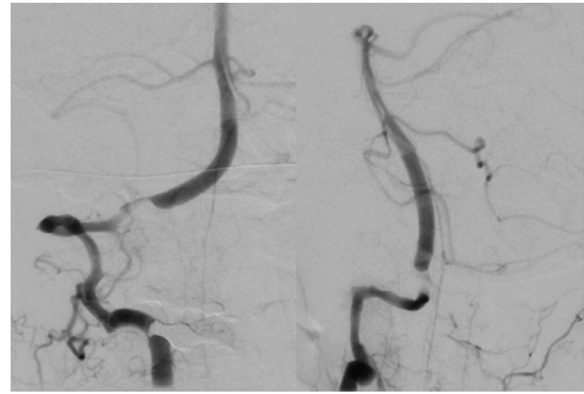
### Case Report

A 39-year-old female with past medical history significant for migraine presented to our emergency room (ER) for worsening headache over 3 days. The characteristics of this episode of headache were similar to her typical migraine headaches, however, the headache was not relieved with over the counter anti-inflammatories. She denied any recent history of trauma, fall, heavy lifting, fever and cough. No other significant past medical/ surgical history. She denied taking any other medications except over the counter pain medications. She denied any family history of connective tissue disorder. On clinical examination, her vital signs and neurologic examination were normal. General physical examination was unrevealing for any evidence of connective tissue disorder. No imaging studies were performed. Nasopharyngeal swab was negative for RNA of novel COVID-19. She was managed with intramuscular ketorolac and oral ondansetron, and was discharged home after partial pain relief.

She returned back to the ER after 2 days with worsening headache associated with pain and tenderness around her neck. Her vital signs and neurologic exam were again normal. Non-contrast CT (computed tomography) head did not reveal any acute abnormality. CT angiography (CTA) of the head and neck showed irregularities and high grade stenoses of V3 segments of bilateral vertebral artery, concerning for dissection (Fig. 1). At this time, she was started on a therapeutic heparin drip. Magnetic resonance imaging (MRI) did not reveal any embolic strokes. The next day, she had digital subtraction angiogram (DSA) to evaluate the extent of dissection and detect high risk features such



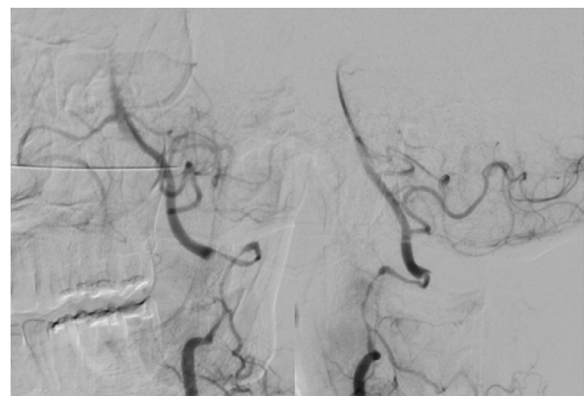
**Fig. 1.** a) There is narrowing and irregularity of the Right V3 segment extending to the V4 segment (orange arrow), resulting in a high-grade stenosis suggestive of dissection. b) Left V3 segment (red arrow) is also markedly irregular and diminutive in caliber, with multiple regions of high-grade stenosis suggestive of dissection.



**Fig. 2.** Diagnostic cerebral angiogram (AP and lateral views) demonstrating Right vertebral artery V3/4 irregularity and stenosis secondary to dissection.

as pseudoaneurysm or thrombus. DSA showed tapering, irregularities and severe stenosis of V3 segments of bilateral vertebral arteries consistent with dissection; on the right side the dissection appeared to extend to the V4 segment. No thrombus or pseudoaneurysm was detected (Figs. 2 and 3). Nasopharyngeal swab to evaluate for COVID-19 was repeated and it came back positive. C-reactive protein was 4 mg/L (reference 0-5), lactate dehydrogenase 157 u/L (reference 120–250), serum ferritin 40 ng/ml (reference 13–150), D-Dimer 224 ng/ml (90–500). Rest of the laboratory findings were also normal.

The options of medical management with anticoagulants or endovascular intervention with stenting were considered and discussed with the patient. We recommended medical management due to the absence of any intracranial hemorrhage, pseudoaneurysm and stroke and the presence of bilateral vertebral artery involvement. The heparin drip was continued with partial thromboplastin time (PTT) in the therapeutic range and was subsequently bridged to therapeutic coumadin. The patient remained neurologically intact. Her repeat CTA after 2 days interval remained unchanged. She did not develop



**Fig. 3.** Diagnostic cerebral angiogram (AP and lateral views) demonstrating Left vertebral artery V3 segment irregularity and stenosis secondary to dissection.

other symptoms such as fever, cough or dyspnea during 6 days of hospitalization.

## Discussion

In this report, we describe a 39-year old female patient with spontaneous bilateral vertebral artery dissections. The patient reported no instigating traumatic events and no history of connective tissue disorders. Her clinical examination also did not reveal her to be suffering from a connective tissue disorder. There was no obvious evidence of fibromuscular dysplasia in carotid arteries on the imaging studies. Whether this patient's vertebral artery dissection was triggered by the exaggerated inflammatory response or arteriopathy secondary to COVID-19 remains speculative at this time. Nonetheless, vascular dissection could be one of the many manifestations of this multi-organ disease.

Cervicocranial arterial dissection is one of the common causes of ischemic stroke among young adults.<sup>11</sup> Oxley et al recently reported a case series of 5 COVID-19 positive patients (mean age of 39 years), with no significant past medical history who presented with stroke secondary to a large vessel occlusion (LVO).<sup>4</sup> With more younger patients who are COVID-19 positive, presenting with strokes during this pandemic, arterial dissection could be one of the pathological mechanisms. Arterial dissection in patients with COVID-19 could be secondary to exaggerated inflammatory response causing endothelial dysfunction.<sup>6</sup> Another potential mechanism could be the direct SARS-CoV-2 invasion of the vascular endothelial cells.<sup>7,8</sup> SARS-CoV-2 uses spike proteins on its surface to bind to the angiotensin-converting enzyme 2 (ACE2) receptors, which are expressed in the vascular endothelium throughout the body.<sup>7,8</sup> This could result in increased chances of vascular endothelial injury in COVID-19.

The management of COVID-19 patients with arterial dissection should continue to be dictated by the clinical examination and imaging studies. We considered medical management and endovascular intervention with stenting/vessel sacrifice in our patient and discussed the options with her. We recommended medical management due to the absence of any intracranial hemorrhage, pseudoaneurysm and stroke and the presence of bilateral vertebral artery involvement. The patient was treated with full dose anticoagulation.

Arterial dissection could be one of the unusual complications of COVID-19 that treating physicians need to be aware of. We recommend that vascular imaging of the head and neck should be an essential component of the work-up in stroke patients who are COVID-19 positive. Head and neck imaging could also be considered in COVID-19 patients who present with unusual and unremitting headaches especially those associated with neck pain. Moreover, the young patients presenting with arterial dissection even in the absence of stroke should be checked for COVID-19.

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