A case series of upper limb ischemia due to thromboembolic complication of COVID-19

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Abstract
Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is a life-threatening multi-organ disease that has swept the globe. Patients with COVID-19 are at an increased risk of thromboembolic consequences involving both the venous and arterial systems, according to growing evidence. Thromboembolic events in COVID are more likely among patients hospitalized to the critical care unit, according to research. However, even in ambulatory and moderate cases of COVID infection, some cases have lately been documented with comparable consequences. D-dimer and fibrinogen levels in the lab can help determine the likelihood of developing thrombotic complications in these patients. This case series discusses about three cases which had similar presentations of coagulopathy of the upper limb arteries associated with COVID infection.

Keywords: COVID-19, coagulopathy, thrombectomy, thrombotic events

Introduction
SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) causes a range of illnesses that primarily impact the respiratory system and frequently involve the haemostatic system. It has been discovered that COVID-19 patients, particularly those with severe disease, have a considerably higher incidence of venous thromboembolism (VTE) [1-4]. Acute pulmonary embolism (PE), deep-vein thrombosis (DVT), ischemic stroke, myocardial infarction, and systemic arterial embolism were among the thromboembolic events. Infection with COVID-19 causes a significant increase in fibrinogen and D-dimer/fibrin (ogen) degradation products. Due to increased gravitational stress and lesser endothelium fibrinolytic activity compared to upper extremity veins, the majority of DVTs develop in the lower extremities (LEDVT). Only 4–10% of Upper limb DVTs (UEDVT) occurs in the upper extremities, and they might be either primary (20%) or secondary (80%) [5-8]. PrimaryUEDVTs, which occur in two out of every 100,000 patients, are either idiopathic or caused by exertional injuries. The link between upper limb deep vein thrombosis (UL-DVT) and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is poorly understood. We discuss three cases that had COVID-19 viral pneumonia as well as acute limb ischemia in the right upper extremity, necessitating open thromboembolectomy with endarterectomy.

Case Report 1
A 37 years old man had fever for one week with upper respiratory tract illness and was found to be COVID-19 positive through RT PCR. He did not have any other symptoms of the viral disease and was treated in home isolation for two weeks. He complained of pain, numbness of the right upper limb and discoloration of index, middle and ring finger for one week which brought him to the hospital. There was no history of diabetes, hypertension or other comorbidities. On clinical examination, he had cold hands and discoloration of middle and index finger, Radial artery pulsation not palpable. The patient was otherwise normal with stable findings on examination. He was investigated with Arterial Doppler and diagnosed with complete thrombosis of axillary, brachial, radial and ulnar arteries in the right upper limb. Blood investigations revealed raised D-dimer levels and other parameters were within normal limits with normal liver and renal function. Digital subtraction angiography (DSA) revealed 2cm clot in right sub-clavian artery and complete thrombosis of axillary, brachial, radial and ulnar arteries.
He underwent digital subtraction angiography (DSA) guided thrombectomy and thrombolysis with 5 mg actylise. Blood flow was restored in brachial, proximal radial and ulnar arteries following the procedure. He was put on tablet Rivoroxaban 20 mg once a day and combination tablet of Clopidogrel + Aspirin 75 mg once a day. His symptoms came down post-operatively and had a full recovery within five days.

**Case Report 2**

A 54 years old woman had fever for one week with upper respiratory tract illness and was found to be COVID-19 positive through RT PCR. He had mild cough and loss of smell and was treated in home isolation five days. He complained of pain, numbness of the left upper limb and discoloration of thumb and middle finger for one week which brought her to the hospital. She was a known case of diabetes and hypertension for the past five years and on regular treatment. On clinical examination, he had cold hands and discoloration of thumb and middle finger, Radial artery pulsation not palpable. The patient was otherwise normal with stable findings on examination. She was investigated with Arterial Doppler and diagnosed with complete thrombosis of axillary, brachial, radial and ulnar arteries in the right upper limb. Blood investigations revealed raised D-dimer and WBCs (14,000) for which he was given a course of antibiotics and a raised Serum creatinine of 1.4. She underwent digital subtraction angiography (DSA) guided thrombectomy and thrombolysis with 5 mg actylise. Blood flow was restored in brachial and radial arteries but ulnar artery did not have flow following the procedure. She was put on tablet Rivoroxaban 20 mg once a day and combination tablet of Clopidogrel + Aspirin 75 mg once a day. Her symptoms came down post-operatively and had a partial recovery within ten days.

**Case Report 3**

A 52 years old woman had fever for one week with upper respiratory tract illness and was found to be COVID-19 positive through RT PCR. He admitted in hospital with saturation 91% and mild dyspnea. He complained of pain, numbness of the right upper limb and discoloration of all fingers for 10 days which brought him to the hospital. He was a known case of diabetes for 8 years and hypertension for the past two years and on regular treatment. On clinical examination, he had cold hands and discoloration of all fingers and radial pulsation not palpable. The patient was otherwise normal with stable findings on examination. He was investigated with Arterial Doppler and diagnosed with complete thrombosis of axillary, brachial, radial and ulnar arteries in the right upper limb. Blood investigations revealed raised D-dimer levels and other parameters were within normal limits with normal liver and renal function. He underwent digital subtraction angiography (DSA) guided thrombectomy and thrombolysis with 5 mg actylise. Blood flow was restored in brachial and radial arteries with ulnar artery showing patchy flow following the procedure. He was put on tablet Rivoroxaban 20 mg once a day and combination tablet of Clopidogrel + Aspirin 75 mg once a day. His symptoms came down post-operatively and had a partial recovery within five days.

### Table 1: D-Dimer levels and CT score in the patients

| Case | SpO2 % | CT score | RTPCR | D-dimer ng/FEU/mL |
|------|--------|----------|-------|-------------------|
| 1    | 99     | 9/25     | +     | 643               |
| 2    | 98     | 11/25    | +     | 650               |
| 3    | 91     | 15/25    | +     | 723               |

**Discussion**

The COVID-19 infections described above all resulted in thrombotic problems in the upper limb. Thrombotic events began in all instances after 10 days of COVID-19 infection. Diabetes and hypertension were common co-morbidities in the majority of the cases. A rise in D-dimers is one of the most typical results in these patients who need to be admitted to the hospital [10]. Based on the existing research, in COVID19 patients with septic coagulopathy, monitoring PT, D-dimer, platelet count, and fibrinogen can be helpful in determining prognosis. If these indications deteriorate, watchful critical care assistance is required, and blood product therapy should be considered whenever possible [10]. If these markers stay the same or improve, it offers more confidence. Several mechanisms have been postulated to explain the pathophysiology of COVID-19-related coagulopathy. Invasion of the vascular endothelium by viruses and endothelitis may play a role. The direct invasion of endothelial cells by the virus using angiotensin-converting enzyme 2 (ACE2) receptors on the endothelial cells and subsequent endothelitis leading to endothelial dysfunction is one major mechanism that culminates in vasoconstriction and end-organ ischemia [11-14]. COVID-19 patients’ endothelial cells have also been found to have viral inclusions. Our patients did not have severe COVID-19, and instead had a moderate condition defined by a low-grade fever and flu-like symptoms that disappeared. Their only presenting symptoms were discoloration and numbness of fingers. In the absence of other important etiologies for peripheral vascular disease, COVID-19 should only be the reason for the direct rise of D-dimer levels and coagulopathy [15]. These cases discussed emphasizes the fact even if they do not have severe COVID-19, people of advanced age with COVID-19 should be monitored for the development of arterial thrombotic problems. Thus prophylaxis for coagulopathy with oral anti-thrombotics or low molecular heparin must be considered by monitoring the D-dimer levels in patients with co-morbidities [16-18]. Though the mechanisms underlying coagulopathy caused by COVID infection are constantly being studied and verified, one thing is certain: meticulous steps must be taken to prevent and treat thrombosis in these high-risk individuals. Guidelines must be developed as soon as possible regarding who must receive intensified anticoagulation therapy during their hospital stay and who will require prolonged anticoagulation therapy after discharge.

**Conclusion**

Our findings show that coagulopathy is present in COVID-19 and is likely to be associated with presence of co-morbidities and elderly age. Because hypercoagulability is linked to a poor prognosis for COVID-19, the trend of hypercoagulability associated with severe COVID-19 should be examined. Contrary to previous accounts in the literature, we provide a case series with three cases that are only mild to moderate disease of COVID-19 but underwent thrombectomy of the radial and ulnar thrombus.

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