

Acute Upper Limb Ischaemia Due to Arterial Thrombosis in a Covid-19 Patient: A Case Report

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Abstract

Case Report

Coronavirus disease 2019 (COVID-19) which is declared as a global pandemic by WHO in March 2020, initially started as a respiratory disease with pneumonia, the cause being the novel coronavirus called as the severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) in Wuhan, China. In addition to respiratory symptoms which were seen initially, the virus is recognized to have different manifestations including seizures, meningitis, diarrhea and coagulopathy. Here we report a case of 60 year old female patient who had dry gangrene of left upper arm due to arterial thrombosis to highlight the association of coagulopathy in patients with mild symptoms of COVID-19.

Keywords: COVID-19, Pandemic, arterial thrombosis.

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INTRODUCTION

In December of 2019, Wuhan, China started reporting multiple cases of pneumonia which in January of 2020 were declared as novel coronavirus disease (COVID-19) caused by a novel coronavirus called as severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) [1]. On March 11, 2020 WHO declared SARS-CoV-2 as a global pandemic [2]. COVID-19 was initially considered to be a respiratory disease with symptoms in the patient ranging from mild fever, dry cough, sore throat to acute respiratory distress syndrome [3]. As of now, other systemic involvement like cardiovascular [4], neurological [5], gastrointestinal [6] are being increasingly recognized as COVID-19 symptoms. The association between coagulopathy and COVID-19 are demonstrated by raised levels of D-dimer and prolonged prothrombin time in severe COVID-19 and by autopsies that show 58% of cases have deep vein thrombosis out of which, 30% cases have fatal venous thromboembolism [7]. The incidence of arterial thrombus is very low in comparison to venous thrombus, but it has been reported in cases of COVID-19. The exact incidence of arterial embolism is yet to be determined, these event range from pulmonary embolism to limb ischaemia [8, 9]. Hypercoagulability is associated with poor prognosis. There is a need to study the trend of hypercoagulability with COVID-19 cases. Here, we present contrary to the reports, a case of elderly female with clinically mild COVID-19 who lost her limb due to thrombosis.

CASE REPORT

A 60 year old female presented to the emergency department with complaints of wound on her left upper limb since 10 days. She also had a history of fever spike (100° F). She had taken preliminary treatment from a local doctor. She observed sudden blackening of her upper limb with foul smell. There was no history of trauma. The patient had no history of smoking or tobacco consumption or history of OC pill intake and did not have any co-morbidities. On examination she was oriented, alert, with increased respiratory rate and oxygen saturation of 90% on room air. Her left hand was blackened from the elbow region with radius and ulna both exposed. Her brachial pulse was palpable. Rapid antigen test done in the emergency department for COVID-19 was negative. Table 1 and 2 represent her laboratory work up.

Table-1: Pre-Operative Laboratory Investigations

TEST	RESULT
Haemoglobin	9.9 g/dl
Total Lymphocyte Count	10.8 (x10 ³ /L)
Red Blood Cells	4.5 (x10 ¹² /L)
Platelets	2.22 (x10 ⁹ /L)
Prothrombin Time	14 secs
D-dimer	856 ng/FEUmL
Urea	23.9 mg/dl
Creatinine	0.8 mg/dl
Sodium	136 mEq/L
Potassium	4.4 mEq/L
CRP	79.2 mg/L

Table-2: Post-Operative Laboratory Investigations

TEST	RESULT
Haemoglobin	9.4 g/dl
Total Lymphocyte Count	13.0 ($\times 10^3$ /L)
Red Blood Cells	4.3 ($\times 10^{12}$ /L)
Platelets	2.1 ($\times 10^9$ /L)
Prothrombin Time	13 secs
D-dimer	638 ng/FEUmL
Urea	23.9 mg/dl
Creatinine	0.8 mg/dl
Sodium	136 mEq/L
Potassium	3.5 mEq/L
CRP	79.2 mg/L

The patient was immediately admitted in the ICU. A central line was inserted in the right internal jugular vein and the patient was planned for left transhumeral amputation on emergency basis. A CT-angiogram of left upper limb was done with a suspicion of thrombus. Oxygen saturation was 98% with 4 litres of oxygen in the ICU. Nasopharyngeal swab was sent for RT-PCR for COVID-19. Surgery was done with closure of the amputation stump. Patient was started on intravenous antibiotics and analgesics and intravenous heparin in the post-operative period. CT-angiogram of left upper limb was suggestive of thrombus of approx 2cm in the proximal left subclavian artery in the second and third part. The RT-PCR report was positive for COVID-19. Blackening of suture line was seen 36 hours after surgery. Total wound gaping was seen on post-operative day 3. Patient was vitally stable on post-operative day 3 and was referred to a higher centre for the management of thrombus due to lack of cardiovascular surgical expertise.

**Fig-1: Pre-operative presentation****Fig-2: Amputation stump****Fig-3: Suture line POD-2****Fig-4: Wound gaping POD-3**

DISCUSSION

Cantador *et al.*, in their study, have shown that out of 1419 COVID-19 patients, 14(1%) patients developed systemic arterial thrombotic events of acute coronary syndrome, acute ischaemic stroke and acute lower limb ischaemia with a mortality rate of 28.6% in the above patients [10]. Similarly, a cohort study in Italy showed an increased incidence of acute limb ischaemia in patients of COVID-19 from January to March 2020 compared to January to March 2019 (16.3% vs. 1.8%, respectively; $p < .001$) [11]. Another observational study showed that 3.7% of critically ill COVID-19 patients have acute arterial thrombotic events [8].

Several mechanisms have been hypothesized to know the pathophysiology of coagulopathy and COVID-19 [12]. A role may be played initially by the viral invasion of vascular endothelium causing endothelitis. One important mechanism that causes vasoconstriction and end-organ ischaemia is the direct invasion of endothelial cells by the virus using angiotensin-converting enzyme 2 (ACE2) receptors on the endothelial cells. This leads to endothelitis leading to endothelial dysfunction. Endothelial cells of COVID-19 patients have shown viral inclusions [13].

Inflammatory cytokines may lead to a hypercoagulable state. Severe COVID-19 is associated with increased production of interleukin-1, interleukin-6 and tumor necrosis factor-alpha [5]. The inflammatory cytokines activate platelets, endothelium and neutrophils, which causes thrombosis [12].

Another mechanism believed to cause coagulation in COVID-19 involves the monocyte, macrophages and neutrophils. Activated monocytes in severe COVID-19 upregulate the tissue factor, which in turn activates the coagulation cascade and thrombosis [12]. Neutrophil extracellular trap generation from abnormally activated neutrophils activates the cytokine storm and thrombosis [13]. Immobility of critically ill patient leads to stasis of blood and hypercoagulability.

Contrary to the literature that shows thrombosis mostly occurs in severe COVID-19 patients, our patient did not have severe COVID-19; instead, she had a mild disease characterized by a low-grade fever that resolved the day before presentation to the emergency department. On presentation, she had no COVID-19 related symptoms; her only presenting signs were dry, shrivelled and blackened left upper limb with both radius and ulna exposed. In this patient, the inflammatory cytokines and activated monocytes and neutrophils did not appear to have a role in the activation of the coagulation cascade leading to arterial thrombosis because the patient was stable both clinically and on laboratory findings. Thus, this case underscores that direct endothelial invasion, damage, and activation caused by SARS-CoV-2 using ACE2

receptors with subsequent coagulation activation is the vital underlying pathophysiological mechanism that leads to the development of thrombosis.

CONCLUSION

This case shows the importance of monitoring elderly patients of COVID-19 for arterial thrombosis even if they do not have severe COVID-19 clinically. We also recommend the stratification of patients with COVID-19 based on their risk of development of arterial thrombosis and the use of prophylactic antithrombotic treatment accordingly.

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