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Case Report

Acute Upper Limb Arterial Thrombosis associated with COVID-19: A Case Report

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A B S T R A C T

COVID-19 is a viral respiratory illness caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Majority of the cases present with upper or lower respiratory tract disease. Common complications of the disease include cytokine storm and acute respiratory distress syndrome. The disease is also found to be associated with an increased incidence of thromboembolism. However, data and literature regarding this dreadful complication are limited. Here, we present a case report of arterial thrombosis in COVID-19 which led to ischemia and gangrene of the fingers.

Keywords: COVID-19, Arterial Thrombosis, Upper Limb Ischemia, Gangrene

Introduction

The novel coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was declared a worldwide epidemic by the World Health Organization on March 11, 2020. COVID-19 case was reported first in December, 2019 in China and since then it has spread across the world with more than 11 crore confirmed cases and more than 25 lakh fatalities.[1] The clinical spectrum of COVID-19 ranges from being asymptomatic to severe forms like acute respiratory distress syndrome (ARDS), sepsis, septic shock, and multiorgan dysfunction syndrome(MODS).[2] As per the Chinese centre for disease control and prevention, it is observed that 81% of the patients, have only mild to moderate disease, 14% have severe disease, while only 5% have critical disease like MODS, shock, and ARDS.[3] Evidence shows that these severe and critical forms are associated with hypercoagulable state with the presence of micro-and macro-vascular thrombotic angiopathy. This evidence is further strengthened by the presence of elevated levels of D-dimer, fibrinogen, and prothrombin in COVID-19 patients.[4,5] Hypercoagulable state in COVID-19 can lead to thrombotic complications including myocardial infarction (MI), ischemic stroke, venous thromboembolism (VTE), limb gangrene, pulmonary thromboembolism, and ischemia affecting bowel, kidney, spleen, and liver. It has been seen that arterial thrombosis has an incidence of 4.4% in severe COVID-19 patients.[6] Still there are limited and scattered studies available on arterial thrombosis in COVID-19. Here, we present a case of a 65-year old diabetic and hypertensive lady diagnosed with severe COVID-19 pneumonia with acute arterial thrombosis in the left upper limb with gangrene formation.

Case Report

A 65-year old female, a known case of hypertension and type 2 diabetes mellitus, presented to the emergency department with complaints of low-grade fever and malaise for 3 days followed by dyspnoea at rest for 1 day with a positive report of nasopharyngeal swab for SARS-CoV-2 virus by RT-PCR test. Diabetes and hypertension were well controlled on medications. There was no history of smoking and alcohol intake. On examination, she had tachycardia (PR-110/min) with a blood pressure of 136/90 mmHg, respiratory rate of 22/min, bilateral infrascapular crackles, and SpO_2 of 86% on room air. Table 1, shows the result of baseline investigations. Chest X- ray showed non-homogeneous opacities in all zones and ECG showed only sinus tachycardia.

Table 1.Baseline Investigations

Parameters	Values
Haemoglobin	14.1 gm/dl
Total leucocyte count (TLC) Differential leucocyte count (DLC)	11240 /dl $P_{90}L_9B_1$
Platelet count	2.39 lakhs/dl
Total bilirubin	0.8 mg/dl
AST/ ALT	40/81 U/L
Alkaline phosphatase	96U/L
Blood urea,/ serum creatinine	58 mg/dl, /0.7 mg/dl
Lactate dehydrogenase	1253 U/L
C-reactive protein	149 mg/l
APTT/ INR	22.9 sec(control 29 seconds), INR 1.21
D-dimer	5000 ng/ml
Serum ferritin	1137 ng/mL
Arterial blood gas	Hypoxemia with normal lactate

She was managed with oxygen therapy, antibiotics, systemic steroid, antioxidants and low molecular weight heparin (prophylactic dose) according to the National COVID-19 guidelines. During the course of the hospital stay the patient developed acute severe pain in the left forearm and hand associated with sensory loss and oedema. On examination, she had cold, localised cyanosis of the left-hand fingers extended to the wrist, absent radial and ulnar pulses, unrecordable SpO_2 in the left-hand fingers, although, no necrotic focus was seen. All other pulses were palpable and no localised discolouration, pain, or tenderness was there in the other extremities. Due to our suspicion of acute limb ischemia, a doppler ultrasound of the left upper limb was conducted which revealed the presence of thrombus in the distal most part of the left subclavian artery and completely filling brachial, axillary, radial and ulnar artery. Also, it showed an echogenic content along the walls of the left upper limb veins with a negligible flow in them suggestive of thrombophlebitis. Echocardiography showed normal ejection fraction and no intracardiac thrombi, tumour or any other abnormality. Doppler ultrasound of neck vessels showed no abnormality. The patient was not having central venous and arterial catheter on the left upper limb and neck. Radiographs of the left forearm and hand were normal. Her thrombophilic screen, ANA, and HIV 1/2 were negative. The presence of sepsis and DIC were ruled out. In the absence of a previous history of such an incident, no recent history of left arm/hand trauma, and no history of atrial fibrillation, she was diagnosed with a possible thrombotic complication secondary to SARS-CoV-2.

Figure 1.Left Upper Extremity of the Patient showing Features of Arterial Thrombosis and Ischemia with Gangrene of Distal Fingers

In view of acute thromboembolism of the left upper limb treatment was updated (anticoagulant-therapeutic heparin infusion and antiplatelet therapy). Despite that the patient developed paresis and peripheral ischemic changes in the left forearm and hand followed by gangrene in fingers in the next 2 days. Surgical Vascular intervention could not be done, as the patient was not fit for surgery because of comorbidities and poor performance status of the patient. During the further hospital stay, there was no improvement in hypoxia and left upper limb ischemia. Repeat doppler ultrasound showed a failure of recanalisation of vessels. Unfortunately, the patient succumbed to COVID related complications:- sepsis and MODS.

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Discussion

COVID-19 is a rapidly spreading disease worldwide. It is associated with various complications including thromboembolism, which is now reported in various studies. Bellosta et al reported a case series of 20 patients with limb ischemia secondary to arterial thrombosis.[7] Fraisse et al reported a 6.5% incidence of arterial thrombosis in COVID-19 patients.[8] A study by Klok et al. documented a cumulative incidence of thrombotic complications of 49% in a cohort of critically ill COVID-19 Dutch patients who were receiving standard doses of thromboprophylaxis.[9] Majority of COVID-19 patients with arterial thrombosis have the following risk factors: pre-existing chronic illness and comorbidities (like, hypertension, diabetes mellitus, atrial fibrillation, chronic kidney disease, dyslipidemia, etc.), age more than 65 years, severe/critical forms of COVID-19, cancer, prior history of thrombosis, thrombophilia, prolonged immobilisation and D-dimer more than 2 times the upper normal limit.[6,10] US registry of patients with COVID-19 has reported thrombotic complications in only 2.6 % of 229 non critically ill hospitalised patients, compared to 35.3% in critically ill hospitalised patients.[11]The patient in our report was elderly, had hypertension, diabetes mellitus, severe COVID-19 pneumonia, and elevated D-dimer levels. A systematic review by Isaac et al documented that 39% of all cases of arterial thrombosis have limb artery involvement.[6] Our case further adds up to that pool.

The mechanisms of arterial thrombosis in COVID-19 patients are still being studied and not completely clear. There is evidence suggesting that presence of direct endothelial damage by the virus (mediated by overexpression of angiotensin-converting enzyme receptor 2), endothelial inflammation, hypercoagulable state (evident by the presence of elevated D-dimer, prothrombin, factor VIII and fibrinogen), higher clot firmness, hyperviscosity, and activation of coagulation cascade (by inflammatory cells and associated cytokines), increased platelet activation, and prolonged immobilisation in critically ill patients, all together add up and provide a possible explanation for thrombosis in COVID-19.[6,10] A study of 115 patients with COVID-19 by Zaid Y et al. showed the presence of SARS-CoV-2 RNA in platelets and elevated platelet associated cytokines.[12]

Regarding mortality in COVID-19 patients with arterial thrombosis, a cohort study by Lodigiani C et al. reported a 20% mortality rate, and that too is mainly due to end-organ injury.[13] This case report adds up that severe COVID-19 disease can also lead to life- threatening acute limb ischemia and gangrene. American College of Chest Physicians (ACCP) suggest prophylaxis with low molecular weight heparin (40 mg once daily dose)for all hospitalised patients with COVID-19 in absence of contraindications, like active bleeding. Patients with COVID-19 diagnosed with arterial or venous thrombosis should be treated as per the treatment guidelines for thrombosis in any other clinical condition. Also, ACCP does not recommend measuring D-dimer to determine the intensity of prophylaxis or treatment.[10]

Conclusion

To conclude, we had a case with COVID-19 infection who developed arterial thrombosis leading to acute ischemia in the left upper limb despite being on thromboprophylaxis with low molecular weight heparin. The treating physicians should be aware of such fatal thromboembolic events associated with COVID-19 so that early and appropriate intervention can be done.

Conflict of Interest: None

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