



COVID 19 BEYOND PNEUMONIA: PRESENTING AS PERIPHERAL GANGRENE - CASE SERIES

General Medicine

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ABSTRACT

The novel coronavirus disease (COVID-19) caused by SARS-CoV-2 has affected the world in every aspect since its onset in 2019. The thrombo-inflammatory complications of this disease are common in critically ill patients and associated with poor prognosis. Our aim was to report the clinical profile and outcome of patients diagnosed with peripheral gangrene (PG) associated with COVID-19. In this case series, we have discussed the clinical presentation, laboratory parameters and outcome in a series of two patients of COVID-19 with peripheral gangrene. Two consecutive patients (both females, age range: 55–77 years, were admitted with the diagnosis of COVID-19, both patients developed peripheral gangrene during their illness. Despite vigorous management, both patients succumbed to their illness within a fortnight of admission. PG in the background of COVID-19 portends a fatal outcome. Clinicians should be alerted to diagnose PG early and be aware of its dismal prognosis in COVID-19 patients.

KEYWORDS

INTRODUCTION

COVID-19 epidemic has surprised world with its extensive manifestations and associated with significant morbidity as well as mortality. Along with characteristic respiratory ailment, COVID-19 has shown various thrombo-inflammatory complications, which are common in critically ill patients and associated with poor prognosis^{1,2}. Thrombotic complications in patients with COVID-19 present in a variety of ways like Venous thromboembolism, Ischemic complications related to thrombosis of arteries of extremity, cerebral, coronary, and visceral arteries.³ Few reports in literature have mentioned dry gangrene in non-vasculopathic patients with severe COVID-19, possibly attributable to consumption coagulopathy and shock^{4,5}. This article consists of two cases of Peripheral Gangrene associated with COVID-19 and provides a comprehensive review of this under-recognized entity associated with critical illness. Our aim is to report the clinical profile and outcome of patients diagnosed with PG associated with COVID-19.

Data regarding demography, symptoms, clinical presentation, past medical history including comorbidities, vascular risk factors, addictions, drug/toxin exposure, family history, time course and evolution of disease were obtained. The patients underwent thorough clinical examination and routine laboratory workup. Relevant investigations like CBC, RFT, LFT, Electrolytes Coagulation profile, d-dimer assay, CRP, LDH and radiological assessment (High resolution computed tomography thorax), Doppler ultrasound were also performed. Consent was taken from both patients.

Case Description

Case 1

A 77 year old, female was presented to our hospital with fever from 4 days and difficulty in breathing from 2 days. History was not suggestive of any comorbidities, regular medication usage and any form of substance abuse. On initial assessment, Patient was conscious oriented and febrile. Respiratory distress was present. SPO2 was 85% on Room air, Pulse rate was 110/min, Respiratory rate was 34/minute and Blood pressure was 126/80 mmhg. On Respiratory System examination bilateral crackles were present. All other systemic examination was unremarkable. On initial evaluation, Cutaneous examination was unremarkable. Peripheral pulses were normally felt. Covid 19 Rapid Antigen test was positive. Laboratory investigation revealed thrombocytopenia, Leukocytosis, prothrombin time, APTT was normal, mildly elevated liver enzymes and serum urea. CRP, LDH and D-dimer was elevated significantly, and D dimer was increased on serial evaluation as shown in Table No.1.

CXR PA View was showing patchy inhomogeneous opacities noted in bilateral mid and lower lung zones; p/o consolidation.

Patient was isolated and managed according to covid 19 standard

protocol. Oxygen support as per requirement, Injection Remdesivir, higher antibiotics, intravenous low dose steroids, and prophylactic anticoagulation (enoxaparin) along with supportive measures was started immediately. Despite ongoing anticoagulation therapy, within 2 days of admission patient developed new onset of blackish discoloration of left lower limb toes, which progressed rapidly up to ankle on next day. Left side Dorsalis pedis artery, Anterior Tibial Artery and Posterior tibial artery pulsation was feeble. Cutaneous necrosis, focal blistering, dyspigmentation, and exfoliation were noted over same area. Arterio- Venous DOPPLER – Left lower limb showed that skin and subcutaneous tissue over entire leg appears thickened and heterogenous. Hypoechoic material was seen partially filling lumen of left Superficial Femoral artery suggestive of partial thrombosis. A hypoechoic material is seen partially filling lumen of Left Popliteal artery, Anterior tibial artery, Posterior tibial artery, Dorsalis pedis artery and gives no color flow, - complete thrombosis. A final diagnosis of peripheral Gangrene associated with COVID-19 was considered. Conservative management was continued in form of iv steroids, anticoagulation (enoxaparin 60 mg BD), oxygen support and supportive measures. despite our best efforts the patient had to underwent above knee amputation and succumbed to severe acute respiratory distress syndrome after 15 days of hospitalization.

Case 2

A 55 year old, female was presented to our hospital with fever from 4 days, cough from 3 days, and difficulty in breathing from 2 days. She also complained of blackish discoloration of skin involving toes on both side from 1 day. History was not suggestive of diabetes or hypertension, no substance abuse or use of any regular medication. On initial assessment, patient was conscious oriented, febrile, respiratory distress was present, SPO2 was 90% on Room air, Pulse rate was 100/min, RR was 30/min, Blood Pressure was 126/80 mmhg. Both Lower limb toes were showing blackish discoloration up to base of toes and equal on both sides. skin overlying was dry and shriveled. On Respiratory System examination bilateral crackles were present. All other systems examination was unremarkable. Bilateral Dorsalis pedis artery, Anterior tibial artery and Posterior tibial artery and popliteal artery pulsation were absent.

Rapid antigen test was NEGATIVE. RT PCR was negative. HRCT Chest- was suggestive of ill-defined multifocal Ground glass opacities are seen in bilateral lung parenchyma suggestive of Viral pneumonia with CORADS -5 and CT Severity score- 13/25.

Laboratory investigation revealed thrombocytopenia, Leukocytosis, prothrombin time was prolonged APTT was also prolonged. Liver enzymes were elevated, and serum urea and creatinine were also raised on serial evaluation. CRP, LDH and D-dimer was elevated significantly, and D dimer was increased on serial evaluation as shown in Table No.2.

Arterio-Venous Doppler was showing hypoechoic material filling lumen of both Common femoral arteries, and both Superficial femoral artery and shows patchy color flow even on lowest PRF setting suggestive of partial thrombosis. Hypoechoic material filling lumen of both Popliteal artery, Anterior tibial artery, Posterior tibial artery, Dorsalis pedis artery and did not give color flow even on lowest PRF setting. –suggestive of COMPLETE THROMBOSIS.

Patient was isolated and managed according to covid 19 standard protocol. Oxygen support as per requirement, Injection Remdesivir, higher antibiotics, iv steroids, and anticoagulation (Unfractionated heparin Bolus and infusion) along with supportive measures was started immediately. Blackening of toes of both feet progressed above feet on next day despite anticoagulation therapy. Patient's general condition was deteriorated, and oxygen requirement was increased quickly. She was put on NIPPV support and then invasive positive pressure ventilatory support. Despite vigorous therapy, patient succumbed to her illness within 5 days of admission.

Both patients were admitted with the diagnosis Of SARS COV-2 pneumonia. During course of covid 19 infection both patients developed Peripheral Gangrene. First case developed peripheral gangrene after hospitalization, despite receiving anticoagulation therapy. Second case had gangrene at the time of admission only. Despite vigorous therapy, first patient had to underwent above knee amputation and second patient succumbed to her illness within 5 days of admission.

DISCUSSION

Coagulation abnormalities and thrombotic manifestations have been increasingly reported in patients with moderate to severe COVID-19 pandemic. Multisystem inflammation and thrombo-inflammation have provided new insights to the management of this pandemic. COVID-19 predisposes patients to a hypercoagulable state. Several mechanisms behind pathogenesis involves, host immune response contributing to vascular endothelial cell injury, inflammation, activation of the coagulation cascade via tissue factor expression, and shutdown of fibrinolysis.^{3,7}

Jenner et al. reported around 56.3% thrombotic events in 2928 critically ill COVID-19 patients in a systematic review³. The cytokine storm triggered by SARS-CoV-2 mediated by IL-6, interferon-gamma, and IL-2 aggravates the prothrombotic state and facilitates hypercoagulability.³

During course of covid 19 management both patients developed Peripheral Gangrene. First case developed peripheral gangrene after hospitalization, despite receiving anticoagulation therapy. Second case had gangrene at time of admission only. Despite vigorous therapy, first patient had to underwent above knee amputation and succumbed to her illness with 15 days of developing gangrene. Second patient succumbed to her illness within 5 days of developing gangrene.

Therapeutic options in SPG are limited and are not evidence based; prompt recognition and early treatment of the underlying cause may be useful. Aggressive antimicrobial coverage with adequate hydration and judicious correction of DIC guided by basic tests of coagulation is the mainstay of therapy. Replenishing depleted coagulation factors in bleeding predominant disease and recombinant protein C, anticoagulants, antithrombin, plasmapheresis, intravenous immunoglobulin, continuous ultrafiltration, and continuous hemofiltration in thrombotic disease have been tried with limited success.^{8,10}

Peripheral Gangrene in case of covid 19 pneumonia is associated with a high rate of amputation among survivors,⁸ as evident in case 1. Mortality is considerably high in PG with leucopenia and ischemic hepatitis (shock liver) being poor prognostic markers and most deaths occur reportedly between 5 and 21 days of the onset of gangrene.⁹

In our patient, COVID-19 related coagulopathy was associated with poor prognosis. Treatments targeting these pathways may need to be considered to improve clinical outcomes and decrease overall mortality due to thrombotic complications.

CONCLUSION

It is important to have a high degree of suspicion for thrombotic complications as patients may rapidly deteriorate in severe cases.

Early recognition of acute limb ischemia, which is a sudden decrease in the perfusion to an extremity, and intervention, can help reduce mortality in patients of COVID 19 and maximize the chance for limb salvage. As delayed etiological evaluation of peripheral gangrene is associated with poor prognosis, it is advisable to do screening for COVID-19 in patients clinically diagnosed with peripheral gangrene.



Fig:1 Case 1 – Peripheral gangrene in Left Foot

Table:1, Investigation Case:1

Tests	Value
S. Urea	89 mg/dl
S. Creatinine	1.29mg/dl
T. Bilirubin	1.2 mg/dl
SGPT	74 IU/L
SGOT	108 IU/L
CRP	96 mg/L
S.LDH	2880 IU/L
D Dimer	1988 ng/ml (Day 1) 2946 ng/ml (Day 3) 4547 ng/ml (Day 5)
S. Sodium	136 mEq/L
S. Potassium	5.2 mEq/L
RBS	128 mg/dl
HB	15 Gm%
Total WBC count	15800/cumm (Day 1) 16000/cumm (Day 3)
Platelet count	246000/cumm (Day 1) 98000/cumm (Day 3)
Differential count	80/18/1/1/0
Prothrombin Time	18.6 sec
INR	1.18
APTT	38 SEC

Table: 2, Case 2 Investigation

Tests	Values
S. Urea	56 mg/dl 84 mg/dl
S. Creatinine	0.96 mg/dl 1.80 mg/dl
T. Bilirubin	1.00 mg/dl
SGPT	270 IU/ml
SGOT	161 IU/ml
CRP	48 mg/L

S.LDH	3770 IU/L
D Dimer	2946-ng/L (Day 1) 3454-ng/L (Day 3) 5243 ng/L (Day 5)
S. Sodium	143 mEq/L
S. Potassium	3.6 mEq/L
RBS	158 mg/dl
HB	10.00 Gm%
Total WBC count	21880/cumm (Day 1) 11700/cumm (Day 3)
Platelet	60000/cumm (Day 1) 53000/cumm (Day 3)
DC	89/9/1/1/0
PT	18.4 sec 20.70 sec
INR	1.27 (Day 1) 1.45 Day 4)
APTT	26.7 sec (Day 1) >1 MIN (Day 4)

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