Case Report

A young COVID-19 patient with mild symptoms and disseminated intravascular coagulation

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Received: 01 September 2020
Revised: 06 October 2020
Accepted: 07 October 2020

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ABSTRACT

COVID-19 pandemic in recent times has emerged as a major contributor to multisystemic thrombosis and related complications. COVID-19 leads to a syndrome of generalised systemic coagulopathy and acquired thrombophilia which manifests itself in the form of arterial, venous and microvascular thrombosis. The pathological mechanisms for COVID-19 induced coagulopathy are yet to be clear however extensive research is underway and multiple insights have emerged recently. Here we report a case of young COVID-19 patient who presented with mild fever but severely deranged coagulation parameters and inflammatory markers. He was managed conservatively with low molecular weight heparin, Fresh frozen plasma, tab HCQS, tab doxycycline, tab ivermectin, tab zinc, tab vitamin C and responded well to treatment. He was later discharged after testing COVID-19 negative. Screening of all confirmed cases for coagulopathy like D-dimer, FDP, platelet count, prothrombin time may be done to identify high risk asymptomatic/mild cases which may cause further decrease in mortality.

Keywords: Disseminated intravascular coagulation, COVID-19, Thrombosis, Coagulopathy

INTRODUCTION

On 31st December 2019, China reported cases of pneumonia of unknown cause related to the human sea food market in Wuhan.1 A novel strain of coronavirus was identified as the causative agent. The virus was later renamed by WHO as SARS-CoV-2 and the disease as COVID-19.2 Since its detection, 35,407,404 confirmed cases and 1,039,406 deaths have been reported from 270 countries. India has reported 6,685,082 cases and 103,569 deaths until at the time of writing this report.3 SARS-CoV-2 is transmitted via respiratory secretions directly through droplets from coughing, sneezing or indirectly through contaminated objects or surfaces as well as close contacts.4 The major presentations of COVID-19 include fever, breathlessness, cough, myalgia, headache, malaise, nausea, vomiting, diarrhea.5 Cases of new-onset seizures, myocardial infarction and neuropathy have also been reported.6-9 A study of series of autopsies conducted at Mount Sinai hospital, New York reported blood clots in the brain, kidney and liver indicating endothelial damage, activation of the coagulation pathway and persistently raised inflammatory markers indicating the additional plausible role of systemic thromboembolism in COVID patients.9 Post-mortem findings in a series of autopsies conducted in northern Italy reported presence of diffuse alveolar damage, hyaline membrane formation, atypical hyperplasia of pneumocytes, presence of platelet-fibrin thrombi in small vessels indicating coagulopathy in majority of the cases.10 The presence of systemic thromboembolism makes way for use of anticoagulants.
such as low-molecular weight heparin in the management of such patients.\textsuperscript{11}

**CASE REPORT**

A 25-year-old male presented to the emergency department with complain of fever since 1 week, headache since 3 days and loss of appetite since 1 day. Fever was low-grade, intermittent in nature which was associated with headache since last three days. He was treated in a local hospital with inj cefotaxime 1g, tab artemether-lumefantrine (80mg/480mg) and tab paracetamol 500 mg before being referred to our hospital. No history of diabetes mellitus, hypertension, pre-existing liver disease or any other chronic illness was present. No history of cough, shortness of breath, vomiting or burning micturition was present. No history of any recent travel or contact with a positive case of COVID-19 was present.

At the time of admission, the patient was conscious, well oriented to time, place and person with GCS E4V5M6. His vitals were, pulse rate 114/min, BP 110/70 mmHg, respiratory rate 23/min, temperature- 99.4°F. On auscultation bilateral normal vesicular breath sounds were heard, heart sounds (S1 and S2) were normal and no murmur was heard. Abdomen was soft, non-tender on palpation with no organomegaly.

He was then subjected to relevant investigations to evaluate the acute febrile illness and his nasal and oropharyngeal swab was tested for COVID-19 infection using RT-PCR. He was subsequently found to be COVID-19 positive.

With the lab parameters as in (Table 1) suggesting an ongoing inflammation and overt disseminated intravascular coagulation on the ISTH criteria, the patient was apparently having only mild fever and headache.\textsuperscript{12}

The patient had overt disseminated intravascular coagulation (DIC) as per the international society of thrombosis and haemostasis (ISTH) criteria for DIC,\textsuperscript{13} but no symptoms or clinical signs of bleeding was present. He was managed conservatively with tab azithromycin 500mg, tab HCQS 400mg, tab zinc 50mg, tab vitamin C 500mg, tab doxycycline 100mg, tab ivermectin, tab paracetamol 500mg, bed rest, oral fluids with close monitoring of his vitals and finger SpO2 levels.

He was started on low molecular weight heparin 40\textsuperscript{µ}g subcutaneous BD for 7 days along with transfusion of fresh frozen plasma. On subsequent days of admission, he remained afebrile with stable vitals and no clinical signs of coagulopathy. On day 7 of admission, significant reduction in D-dimer levels, rise in platelet counts and normalization of fibrinogen levels were observed.

**DISCUSSION**

COVID-19 in severe cases leads to development of a widespread generalised systemic inflammatory response affecting the blood vessels, lungs, heart, kidney, brain including the small bowel. This predisposes to thrombosis of arteries, veins and the microvascular system. ACE-2 receptors are widely expressed in the vascular endothelium. Montiel et al demonstrated engineered human blood vessel organoids can be infected with SARS-CoV-2.\textsuperscript{13} Inflammatory cells and viral inclusions have been found in the endothelium of heart, small bowel, kidneys and lungs.\textsuperscript{14} Multiple mechanisms such as endothelitis, hyperinflammation, neutrophil extracellular traps (NETs), increase of VWF and factor VIII (indicating multi-fold activation of vascular endothelium) due to unregulated immune response have also been suggested.\textsuperscript{15-17} Tang et al in their retrospective study in Wuhan, China concluded that DIC is a frequent occurrence in the background of worsening COVID-19 pneumonia and is often associated with increased risk of mortality. Significantly higher levels of D-dimer, fibrin degradation product (FDP), prolonged prothrombin time and activated thromboplastin time were reported among the non-survivors. They reported that 71.4\% and 0.6\% non-survivors and survivors respectively met the criteria of disseminated intravascular coagulation. They also suggested anticoagulant therapy with low molecular weight heparin for 1 week was associated with better prognosis in severe cases of COVID-19 meeting the

| Table 1: Investigations on day 1, 7 and 10. |
|-------------------------------------------|
| **Lab Parameters** | **Day 1** | **Day 7** | **Day 10** |
|--------------------|-----------|-----------|-----------|
| Hemoglobin | 9.5 g/dl | 9.8 g/dl | 9.6 g/dl |
| Total Leucocyte count | 3800/mm\(^3\) (N63L34M2E1B0) | 4020/mm\(^3\) (N31L46M4E2B0) | 4600/mm\(^3\) (N4L34M2E1B0) |
| Platelet count | 0.9 lac/mm\(^3\) | 1.75 lac/mm\(^3\) | 1.8 lac/mm\(^3\) |
| Blood Urea | 18.2 mg/dl | 16 mg/dl | 16 mg/dl |
| Serum Creatinine | 0.6 mg/dl | 0.6 mg/dl | 0.5 mg/dl |
| SGOT | 126 U/L | 395 U/L | 234 U/L |
| SGPT | 54 U/L | 235 U/L | 156 U/L |
| SAP | 81 U/L | 144 U/L | 132 U/L |
| Total Bilirubin | 1.1 mg/dl | 0.4 mg/dl | 0.6 mg/dl |
| S. D-dimer | 4.3 \(\mu\)g/ml | 0.8 \(\mu\)g/ml | 0.6 |
| S. Ferritin | >1000 ng/ml | 841 ng/ml | 584 ng/ml |
| S. LDH | 710 U/L | 576 U/L | 468 U/L |
| PT/INR | 15.6 s / 1.22 | 15.4 s / 1.21 | 15.4 s / 1.21 |
| Chest Xray PA view | Both lung fields clear | Both lung fields clear | Both lung fields clear |
| CRP | 91.66 mg/L | 52.42 mg/L | 36 mg/L |
ISTH DIC criteria or those with significantly raised D-dimer levels. Zhou et al in their study reported D-dimer levels>1ug/ml to be poor prognostic indicator of COVID-19 infection. Helms et al studied the occurrence of thrombotic events in 150 patients with COVID-19 pneumonia and ARDS. They reported a higher incidence of pulmonary embolism (16.1%) in COVID-19 associated ARDS compared to 2.1% in non-COVID-19 associated ARDS. Median D-dimer levels of 0.21μg/L in mild cases and 0.49 μg/L in severe COVID-19 cases was reported in a Chinese study.

ACE-2 receptors are also expressed on bile duct epithelial cells which is responsible for liver function abnormality in COVID-19 patients. Chen et al reported varying degrees of deranged liver function tests in 43 out of 99 patients in their study. One patient was reported to have severe liver dysfunction with AST 1445 U/L and ALT 7590U/L. Zhenyu Fan et al in their retrospective study of 148 confirmed COVID-19 patients reported 37.2% cases had deranged liver function. In their study, 57.8% cases with deranged liver function had received lopinavir/ritonavir after admission. Our patient was non-alcoholic, had no history of pre-existing liver disease and any drug intake including lopinavir/ritonavir. Deranged liver function was attributed to COVID-19 for which he was managed conservatively.

In our patient, despite showing no clinical signs and symptoms of coagulopathy, his elevated D-dimer levels, thrombocytopenia, raised ferritin levels, raised LDH levels, mildly elevated prothrombin time were suggestive of an ongoing severe systemic inflammatory immune response. Therefore, contemplating a high risk of progression to severe disease, he was immediately started with anticoagulant therapy with low molecular weight heparin. Screening of these parameters at the time of admission was helpful for us in identifying the probable high risk of progression to severe disease.

Majority of the studies regarding thromboprophylaxis in patients with COVID-19 have been conducted in critically ill patients. Evidence relating to prophylaxis in non-critically ill COVID-19 patients is rather scarce. Also, there is limited evidence for supporting approach to thromboprophylaxis other than the existing regimens for non-critically ill patients. ISTH criteria for DIC has been recommended as a prognostic tool and to guide treatment in severe COVID-19 cases. A consensus statement from Chinese investigators also highlighted the importance of thromboprophylaxis and monitoring of thrombotic complications in patients with COVID-19. The anticoagulation forum recommends evidence based pharmacological prophylaxis, whenever possible in hospitalized COVID-19 patients with dose escalation for the critically ill. They also recommend post-discharge prophylaxis for patients with high risk of VTE.

**CONCLUSION**

Routine screening of confirmed COVID-19 cases for coagulopathy using d-dimer, prothrombin time/INR, fibrinogen, platelet counts may be considered to identify high risk asymptomatic cases. A clinical scoring system may be put in use to assess the risk of progression of asymptomatic cases to severe COVID-19. Empirical use of anticoagulation for hospitalised patients even in the absence of documented or clinically suspected thrombosis should be considered as recommended by various forums.

**Funding:** No funding sources

**Conflict of interest:** None declared

**Ethical approval:** Not required

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