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Case Report

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

Abhishek Kumar*, Piyush Kumar, Ajit Dungdung

Department of Medicine, Rajendra Institute of Medical Sciences, Ranchi, Jharkhand, India

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***Correspondence:**
Dr Abhishek Kumar,
E-mail: abhi.nrs.124@gmail.com

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 hunan 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.[6-8] A study of series of autopsies conducted at Mount Senai 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 thrombo-embolism 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.[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 cefoperazone 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.

Table 1: Investigations on day 1, 7 and 10.

Lab Parameters	Day 1	Day 7	Day 10
Hemoglobin	9.5g/dl	9.8 g/dl	9.6 g/dl
Total Leucocyte count	3800/mm^3 (N63L34 M2E1B0)	4020/mm^3 (N31L46M 19E2B0.5)	4600/mm^3 (N44L42M 11E3B0)
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 µg/ml	0.8 µg/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

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.[12]

The patient had overt disseminated intravascular coagulation (DIC) as per the international society of thrombosis and haemostasis (ISTH) criteria for DIC.[12] 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 40µg 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.[13] Inflammatory cells and viral inclusions have been found in the endothelium of heart, small bowel, kidneys and lungs.[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.[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

ISTH DIC criteria or those with significantly raised D-dimer levels.[18] Zhou et al in their study reported D-dimer levels>1ug/ml to be poor prognostic indicator of COVID-19 infection.[19] 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.[20] 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.[21]

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.[22,23] 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.[24] Our patient was non-alcoholic, had no history of pre-existing liver disease 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 (https://b-s-h.org.uk/). A consensus statement from Chinese investigators also highlighted the importance of thromboprophylaxis and monitoring of thrombotic complications in patients with COVID-19.[25] 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.[26]

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.

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REFERENCES

1. World Health Organization. Pneumonia of unknown cause—China. 2020. Available at: https://www.who.int/csr/don/05-january-2020-pneumonia-of-unkown-cause-china/en/. Accessed on 07 May 2020
2. World Health Organization. WHO Director-General's remarks at the media briefing on 2019-nCoV on 11 February 2020. Available at: https://www.who.int/dg/speeches/detail/whodirector-general-s-remarks-at-the-media-briefing-on-2019-ncovon-11-february-2020. Accessed 20 February 2020.
3. Covid19.who.int. 2020. WHO Coronavirus Disease (COVID-19) Dashboard. Available at: https://covid19.who.int/table. Accessed on 02 February 2020.
4. Lotfi M, Hamblin MR, Rezaei N. COVID-19: Transmission, prevention, and potential therapeutic opportunities. Clin Chim Acta. 2020;508:254-266.
5. Wang Y, Wang Y, Chen Y, Qin Q. Unique epidemiological and clinical features of the emerging 2019 novel coronavirus pneumonia (COVID-19) implicate special control measures. J Med Virol. 2020;92(6):568-76.
6. Asadi-Pooya AA, Simani L. Central nervous system manifestations of COVID-19: A systematic review. J Neurol Sci. 2020;413:116832.
7. Stefanini GG, Montorfano M, Trabattoni D, Andreini D, Ferrante G, Ancona M, et al. ST-Elevation Myocardial Infarction in Patients With COVID-19: Clinic Angiograp Outcom. Circulat. 2020;141(25):2113-6.
8. Montalvan V, Lee J, Bueso T, De Toledo J, Rivas K. Neurological manifestations of COVID-19 and other coronavirus infections: A systematic review. Clin Neurol Neurosurg. 2020;194:105921.
9. Bryce C, Grimes Z, Pujadas E, Ahuja S, Beasley MB, Albrecht R, et al. Pathophysiology of SARS-CoV-2: targeting of endothelial cells renders a complex disease with thrombotic microangiopathy and aberrant immune response. The Mount Sinai COVID-19 autopsy experience. Med Rxiv. 2020.

10. Carsana L, Sonzogni A, Nasr A, Rossi RS, Pellegrinelli A, Zerbi P, et al. Pulmonary post-mortem findings in a series of COVID-19 cases from northern Italy: a two-centre descriptive study. Lanc Infect Diseas. 2020.
11. Kow CS, Hasan SS. Use of low-molecular-weight heparin in COVID-19 patients. J Vasc Surg Venous Lymphat Disord. 2020;8(5):900-1.
12. Kinasewitz GT, Zein JG, Lee GL, Nazir SA, Taylor FB Jr. Prognostic value of a simple evolving disseminated intravascular coagulation score in patients with severe sepsis. Crit Care Med. 2005;33(10):2214-21.
13. Monteil V, Kwon H, Prado P, Hagelkrüys A, Wimmer RA, Stahl M, et al. Inhibition of SARS-CoV-2 Infections in Engineered Human Tissues Using Clinical-Grade Soluble Human ACE2. Cell. 2020;181(4):905-13.
14. Sharma A, Garcia G, Arumugaswami V, Svendsen CN. Human iPSC-Derived Cardiomyocytes are Susceptible to SARS-CoV-2 Infection. Bio Rxiv [Preprint]. 2020:2020.
15. Brill A, Fuchs TA, Savchenko AS, Thomas GM, Martinod K, De Meyer SF, et al. Neutrophil extracellular traps promote deep vein thrombosis in mice. J Thromb Haemost. 2012;10(1):136-44.
16. Escher R, Breakey N, Lämmle B. Severe COVID-19 infection associated with endothelial activation. Thromb Res. 2020;190:62.
17. Becker RC. COVID-19 update: COVID-19-associated coagulopathy. J Thromb Thrombolysis. 2020;50(1):54-67.
18. Tang N, Li D, Wang X, Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J Thromb Haemost. 2020;18(4):844-7.
19. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lanc. 2020;395(10229):1054-62.
20. Helms J, Tacquard C, Severac F, Leonard-Lorant I, Ohana M, Delabranche X, et al. CRICS TRIGGERSEP Group (Clinical Research in Intensive Care and Sepsis Trial Group for Global Evaluation and Research in Sepsis). High risk of thrombosis in patients with severe SARS-CoV-2 infection: a multicenter prospective cohort study. Intens Car Med. 2020;46(6):1089-98.
21. Gao Y, Li T, Han M, Li X, Wu D, Xu Y, et al. Diagnostic utility of clinical laboratory data determinations for patients with the severe COVID-19. J Med Virol. 2020;92(7):791-6.
22. Chai X, Hu L, Zhang Y, Han W, Lu Z, Ke A, et al. Specific ACE2 expression in cholangiocytes may cause liver damage after 2019-nCoV infection. biorxiv. 2020 Jan 1.
23. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lanc. 2020;395(10223):507-13.
24. Fan Z, Chen L, Li J, Cheng X, Yang J, Tian C, et al. Clinical Features of COVID-19-Related Liver Functional Abnormality. Clin Gastroenterol Hepatol. 2020;18(7):1561-6.
25. Zhai Z, Li C, Chen Y, Gerotziafas G, Zhang Z, Wan J, et al. Prevention Treatment of VTE Associated with COVID-19 Infection Consensus Statement Group. Prevention and Treatment of Venous Thromboembolism Associated with Coronavirus Disease 2019 Infection: A Consensus Statement before Guidelines. Thromb Haemost. 2020;120(6):937-48.
26. Barnes GD, Burnett A, Allen A, Blumenstein M, Clark NP, Cuker A, et al. Thromboembolism and anticoagulant therapy during the COVID-19 pandemic: interim clinical guidance from the anticoagulation forum. J Thromb Thrombol. 2020;50(1):72-81.

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