

Late thromboembolic complications after asymptomatic covid-19 infections – A case series.

¹Dr. Shilpa A Rao, Professor, Department of General Surgery, Seth Gordhandas Sunderdas Medical College & King Edward Memorial Hospital Parel Mumbai 400012.

²Dr. Aditya Kunte, Senior Resident, Department of Surgical Gastroenterology, Seth Gordhandas Sunderdas Medical College & King Edward Memorial Hospital Parel Mumbai 400012.

³Dr. Sridhar Suresh, Assistant Professor, Department of General Surgery, Seth Gordhandas Sunderdas Medical College & King Edward Memorial Hospital Parel Mumbai 400012.

⁴Dr. Sakina Hussain, Senior Resident, Department of General Surgery, Seth Gordhandas Sunderdas Medical College & King Edward Memorial Hospital Parel Mumbai 400012.

⁵Dr. Tanvi Dalal, Junior Resident, Department of General Surgery, Seth Gordhandas Sunderdas Medical College & King Edward Memorial Hospital Parel Mumbai 400012.

Corresponding Author: Dr. Sridhar Suresh, Assistant Professor, Department of General Surgery, Seth Gordhandas Sunderdas Medical College & King Edward Memorial Hospital Parel Mumbai 400012.

How to citation this article: Dr. Shilpa A Rao, Dr. Aditya Kunte, Dr. Sridhar Suresh, Dr. Sakina Hussain, Dr. Tanvi Dalal, “Late thromboembolic complications after asymptomatic covid-19 infections – A case series”, IJMACR- February - 2023, Volume – 6, Issue - 1, P. No. 297 – 301.

Open Access Article: © 2023, Dr. Sridhar Suresh, et al. This is an open access journal and article distributed under the terms of the creative commons attribution license (<http://creativecommons.org/licenses/by/4.0>). Which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Coronavirus disease 2019 (COVID-19), caused by a novel severe acute respiratory syndrome SARS-CoV-2 virus, has spread globally creating a pandemic. It has been suggested that corona virus, like some other viruses, may also have significant impact on the hemostatic and haemostatic systems resulting in thrombotic and bleeding complications. The mechanism of coronavirus disease producing a thrombotic event is very complex. To simplify the mechanism, it potentially happens as a response to

endothelial cellular injury and dysfunction, venous stasis due to prolonged immobilization in critical care patients and secondary to prolonged hypoxia.

We have here documented a series of 8 cases which developed Venous thromboembolism post Coronavirus Disease and discussed their outcome.

Keywords: Thromboembolism, VTE, Corona Virus, Covid-19, SARS-CoV-2, Venous, Arterial

Introduction

Infectious complications in critically ill patients are known to activate multiple systemic coagulation and

inflammatory responses that are vital for host defence but can lead to DIC.

Viruses and their components induce the expression of numerous products, including tissue factor on monocytes and macro phages, by binding to pattern-recognizing receptors on

immune cells. The triggering of host inflammatory reactions also results in increased production of pro inflammatory cytokines that have pleiotropic effects, including activation of coagulation, which, if not checked, can lead to consumptive coagulo pathy.¹

As humanity is gaining more knowledge about the Corona Virus disease, its mechanism of action for Throm bo embolism and the ways to prevent it, one way to gain efficiency in gaining knowledge is to well document each case. Hence here we share a case series of 8 patients we encountered in our practice with previous history of Covid-19 and presented with Throm bo embolic episodes.

Case Presentation

Here in all the patients discussed some of them has significant history of Covid -19 infection, and some of them did not have a history of infection with Covid-19, but all the patients here showed significant raised titres of Covid Antibody.

Case 1

A 44-year-old male patient came with complaint of pain and swelling of right lower limb for 3 days. Patient was diagnosed to have right lower limb deep venous Throm bosis on venous doppler suggestive of subacute to chronic lumen occluding thrombus

in distal Inferior vena cava with bilateral Common iliac vein, External iliac vein extending into left Femoral vein, Sapheno femoral junction, Popliteal vein, Anterior Tibial Vein and Posterior Tibial Vein. For which he was

started on Low molecular weight Heparin and Warfarin. He had no symptoms of breathlessness, cough, fever or no recent COVID contact. The patient was worked up for Coagulation studies, which were normal.

His Chest X-ray was normal. He was tested Covid-19 negative on RT-PCR although his SARSCoV-2 Antibody was raised to 2.28. The patient improved symptom matically and was discharged with INR of 1.98.

Case 2

A 60-year-old male patient came with complain to fab dominal pain since 1 week.

There was no history of vomiting, ab dominal distension, obstipation and constipation. His chest X-ray was normal, RT-PCR for Covid was negative and SARCoV-2-Antibody level was raised to 6. He was diagnosed with Is Chae mic bowel disease on CT Angio graphy which revealed Partiallu men occluding thrombus in superior mesenteric artery with oedematous changes in bowel mucosa and sub mucosa. He was conservatively managed. He was previously admitted in May 2020 in medicine ward for Covid - 19 main tainingsa turation on face mask. The stay was uneventful and patient was discharged within 15 days. He also has history of Cerebro-vascular accident in June 2020 for which he was started on Aspirin.

During this admission by day 4 the patient was to lerating oral fluids and was passing flatus

And stools. His Abdomen was soft, non-tender on per Abdo men examination. On day 5, the Patient developed sudden onset achy cardia with hypo tension and was diagnosed

Pulmonary Throm bo embolism. He was trans ferred to medicine Where he expired on 29/9/30.

Case 3

A 57-year-old male patient came with complaints of abdominal distension and

Constipation with obstipation for 4 days. He was diagnosed to have Ischaemic Bowel

Disease on CT scan which showed a Complete lumen occluding thrombus in the SMA with non-enhancement of small bowel. His Chest X-ray was normal, RT-PCR for covid-19 was negative and his SARSCoV-2 Antibody level was raised to 57.29. The patient underwent emergency exploratory laparotomy on 22/ 9/ 2020.

Intra operatively the patient had 70cm of gangrenous bowel which was resected with jejunio-ileal anastomosis. Post-operative period uneventful and patient was started on full diet from post-operative day 6. No comorbidities, any symptoms of COVID present. Patient was started on unfractionated heparin and discharged on Warfarin after 2 weeks.

Case 4

A 60-year-old male patient with complaint of blackening of left lower limb for 8 days was diagnosed to have dry gangrene with acute arterial thrombus of the limb on colour doppler scan which specifies acute complete lumen occluding thrombus in distal Sapheno-femoral junction and Popliteal artery. His Chest X-ray had mild consolidation of left lung. He was RT-PCR for Covid-19 negative but his SARSCoV-2 Antibody level was raised to 52.61. He underwent Left Above Knee amputation on 21/ 9/ 20. Post operatively wound healthy.

Patient discharged eventually with follow up in Chest medicine department advised.

Case 5

A 52-year-old diabetic and hypertensive female had complaints of pain and inability to walk for 7 days. She

was diagnosed to have left lower limb DVT on Doppler scan which revealed Chronic thrombus in Common femoral artery extending up to Anterior tibial artery and started on anticoagulation. Her Chest X-ray was normal with no history of covid in the past. Her RT-PCR for covid was negative and SARCOV-2 Antibody was raised to 3.19. The patient developed warfarin toxicity on day 10 which was treated with vitamin K injections and prothrombin complex concentrate. Once the PT-INR normalized, patient was started on oral Dabigatran and discharged with PT-INR of 2.14.

Case 6

A 34-year-old male patient came with complaints of swelling and pain in left lower limb for 10 days. He was diagnosed with left lower limb DVT and started on anticoagulation. His Doppler scan revealed Acute complete lumen occluding thrombus within Sapheno-femoral vein and popliteal vein. His Chest X-ray was Normal and present RT-PCR for

Covid - 19 was negative. His SARCOV-2 Antibody level was raised to 1.5. He has past history of COVID positive in August 2020 for which he was home quarantined. The patient was symptomatically better and discharged after one week.

Case 7

A 62-year-old diabetic male came with complaints of acute abdominal pain since 2 days with obstipation and constipation. He was diagnosed with Ischaemic Bowel Disease on CT Angiography which revealed partial lumen occluding thrombus of Superior mesenteric artery. His Chest X-ray was Normal and present RT-PCR for covid-19 was negative. His SARCOV-2 Antibody level was raised to 14.68. Intra-operatively patient had gangrene of caecum and ascending colon which was resected and a double-barrelled colonostomy done.

Patient was on full diet on postoperative day 5 and was discharged. He had no history of COVID symptoms or contact.

Case 8

A 64-year-old male came with complaint of numbness in right lower limb for 1 week. He was diagnosed to have a chronic thrombus in Sapheno-femoral artery in Doppler. His Chest X-ray was Normal and present RT-PCR for COVID-19 was negative. His SARS-CoV-2 Antibody level was raised to 10.68. He was given a trial of unfractionated Heparin but the limb started developing gangrene. The patient underwent right above knee amputation. Postoperatively the stump healed well and patient was discharged.

Discussion

Severe acute respiratory syndrome coronavirus 2, coronavirus disease 2019 (COVID-19)-induced infection can be associated with a coagulopathy, findings consistent with infection-induced inflammatory changes as observed in patients with disseminated intravascular Coagulopathy (DIC). The lack of prior immunity to COVID-19 has resulted in large numbers of infected patients across the globe and uncertainty regarding management of the complications that arise in the course of this viral illness. The initial coagulopathy of COVID-19 presents with prominent elevation of D-dimer and fibrin/fibrinogen degradation products, whereas abnormalities in prothrombin time, partial thromboplastin time, and platelet counts are relatively uncommon in initial presentations. Coagulation test screening, including the measurement of D-dimer and fibrinogen levels, is suggested.¹

It was also reported that severity of the SARS-CoV-2 infection was associated with increased VTE risk^{2,3,4}

Pharmacological Thromboprophylaxis has shown promise in preventing venous thromboembolism (VTE) for high-risk individuals. In acutely ill hospitalized patients, the incidence of VTE ranges from 5% to 15%, and can be effectively reduced by one-half to two-thirds with appropriate Thromboprophylaxis.⁵ In critically ill patients, the incidence of deep vein thrombosis (DVT) ranges from 13% to 31% without thromboprophylaxis.⁶ Similarly, the risk may be reduced to 10.9% to 15.5% with low molecular weight heparin (LMWH) or low-dose unfractionated heparin (UFH).^{7,8,9,10}

Patients with coronavirus disease 2019 (COVID-19) pneumonia may be predisposed to thrombotic complications due to excess inflammatory response, endothelial dysfunction, platelet activation, and stasis of blood flow.¹¹ In view of the increased risk of VTE among patients hospitalized for COVID-19 pneumonia, current guidance statements recommend the use of standard-dose thromboprophylaxis with UFH or LMWH.¹²

Conclusion

We hence conclude that thromboprophylaxis has to be a norm in all COVID patients unless it is contraindicated. More attempt to document and present different cases has to be made.

References

1. Jean M. Connors, Jerrold H. Levy. COVID-19 and its implications for thrombosis and anti-coagulation. Blood First Edition 27 April 2020. DOI 10.1182/blood.2020.006000.
2. Xu JF, Wang L, Zhao L, Li F, Liu L, Zhang L, Li Q, Gu J, Liang S, Zhao Q, et al. Risk assessment of venous thromboembolism and bleeding in COVID-19

[published online March 24, 2020]. Res Square Pulmonol. doi:10.21203/rs-18340/v1

3. Tang N, Bai H, Chen X, Gong J, Li D, Sun Z. Anti-coagulant treatment is associated with decreased mortality in severe corona virus disease 2019 patients with coagulopathy. *J Thromb Haemost.* 2020; 18:1094–1099. doi:10.1111/jth.14817

4. Cui S, Chen S, Li X, Liu S, Wang F. Prevalence of venous Thromboembolism in patients with severe novel corona virus pneumonia. *J Thromb Haemost.* 2020; 18: 1421–1424. doi: 10.1111/jth.14830

5. Tapson, V.F.; Decousus, H.; Pini, M.; Chong, B.H.; Froehlich, J.B.; Monreal, M.; Spyropoulos, A.C.; Merli, G. J.; Zotz, R.B.; Bergmann, J.F.; et al. Venous Thromboembolism prophylaxis in acutely ill hospitalized medical patients: Findings from the International Medical Prevention Registry on Venous Thromboembolism. *Chest* 2007, 132, 936–945.

6. Geerts, W.; Cook, D.; Selby, R.; Etchells, E. Venous Thromboembolism and its prevention in critical care. *J. Crit. Care* 2002, 17, 95–104.

7. Cade, J.F. High risk of the critically ill for venous thromboembolism. *Crit. Care Med.* 1982, 10, 448–450.

8. Kapoor, M.; Kupfer, Y.Y.; Tessler, S. Subcutaneous heparin prophylaxis significantly reduces the incidence of venous thromboembolic events in the critically ill. *Crit. Care Med.* 1999, 27, A69. *J. Clin. Med.* 2020, 9, 2489 15 of 17

9. Fraise, F.; Holzapfel, L.; Couland, J.M.; Simonneau, G.; Bedock, B.; Feissel, M.; Herbecq, P.; Pordes, R.; Poussel, J.F.; Roux, L. Nadroparin in the prevention of deep vein Thrombosis in acute decompensated COPD. The Association of Non-University Affiliated Intensive Care Specialist Physicians of France. *Am. J. Respir. Crit. Care Med.* 2000, 161, 1109–1114.

10. Chi, G.; Gibson, C.M.; Kalayci, A.; Cohen, A.T.; Hernandez, A.F.; Hull, R.D.; Kahe, F.; Jafarizade, M.; Sharfaei, S.; Liu, Y.; et al. Extended-duration betrixaban versus shorter-duration enoxaparin for venous Thromboembolism prophylaxis in critically ill medical patients: An APEX trial sub study. *Intensive Care Med.* 2019, 45, 477–487.

11. Bikdeli, B.; Madhavan, M.V.; Jimenez, D.; Chuich, T.; Dreyfus, I.; Driggin, E.; Nigoghossian, C.; Angelino, W.; Madjid, M.; Guo, Y.; et al. COVID-19 and Thrombotic or Thromboembolic Disease: Implications for Prevention, Antithrombotic Therapy, and Follow-Up: JACC State-of-the-Art Review. *J. Am. Coll. Cardiol.* 2020, 75, 2950–2973.

12. Gerald Chi, Jane J. Lee, Adeel Jamil, Vamsi Krishna Gunnam et al. Venous Thromboembolism among Hospitalized Patients with COVID-19 Undergoing Thrombo prophylaxis: A Systematic Review and Meta-Analysis. *J. Clin. Med.* 2020, 9, 2489.