Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Thrombosis Research 192 (2020) 27–28

Contents lists available at ScienceDirect

Thrombosis Research

journal homepage: www.elsevier.com/locate/thromres

Letter to the Editors-in-Chief

Deep venous thrombosis in a non-critically ill patient with novel COVID-19 infection

To the Editor

A 48-year-old non-smoker male with a history of coronary artery disease and non-heart-beating renal donation secondary to hypertensive nephrosclerosis was admitted to the medicine service with subjective fevers, myalgias, non-productive cough and dyspnea for two weeks. He denied recent travel or exposure to persons with known or suspected coronavirus disease 2019 (COVID-19). He had a temperature of 38.9C (102.1F), blood pressure of 187/110 mmHg, and oxygen saturation of 99% on room air. Physical examination was unremarkable except for a surgical scar in the right lower abdominal quadrant. Laboratory testing on admission was notable for leukopenia, thrombocytopenia, and elevated C-reactive protein and D-dimer (Table 1). Polymerase chain reaction (PCR) testing for COVID-19 infection was positive. Chest x-ray demonstrated small patchy opacities in the mid-left lung field and electrocardiogram was remarkable for normal sinus rhythm with a QTc interval of 449 milliseconds. He was started on hydroxychloroquine for COVID-19, as well as azithromycin and ceftriaxone for community-acquired pneumonia. He received enoxaparin for deep vein thrombosis (DVT) prophylaxis. His symptoms improved, he did not require supplemental oxygen, and was discharged on hospital day two.

He presented to the emergency room (ER) three days later with difficulty bearing weight on his right leg. Laboratory testing did not reveal significant changes from prior admission. He had normal range of motion, the leg did not appear erythematous or swollen on physical examination and he was discharged from the ER. The possibility of a deep venous thrombosis was not considered. Approximately two weeks after initial hospital admission, he returned to the ER with worsening right leg pain, erythema, and edema. Pain was sharp in nature, exacerbated by movement, ten out of ten on the numeric pain scale. Acetaminophen did not ameliorate the pain. He was afebrile and saturating 96% on room air. Physical examination was remarkable for erythema of the right leg from mid-calf to thigh and tenderness to palpation. Distal pulses were intact. He was found to have an elevated D-dimer, and COVID-19 PCR was positive again (Table 1). Repeat chest x-ray was remarkable for worsening bilateral opacities. Duplex ultrasound of the right leg demonstrated an acute partially occlusive deep vein thrombosis within the common femoral and popliteal veins and acute occlusive clot in the gastrocnemius vein (Fig. 1). He was started on therapeutic apixaban and IV vancomycin and ampicillin/sulbactam for possible overlying cellulitis. Further coagulation studies revealed a normal fibrinogen (313 mg/dL), and negative beta glycoprotein IgM/IgG, cardiolipin IgM/IgG and lupus anticoagulant. Erythema and pain

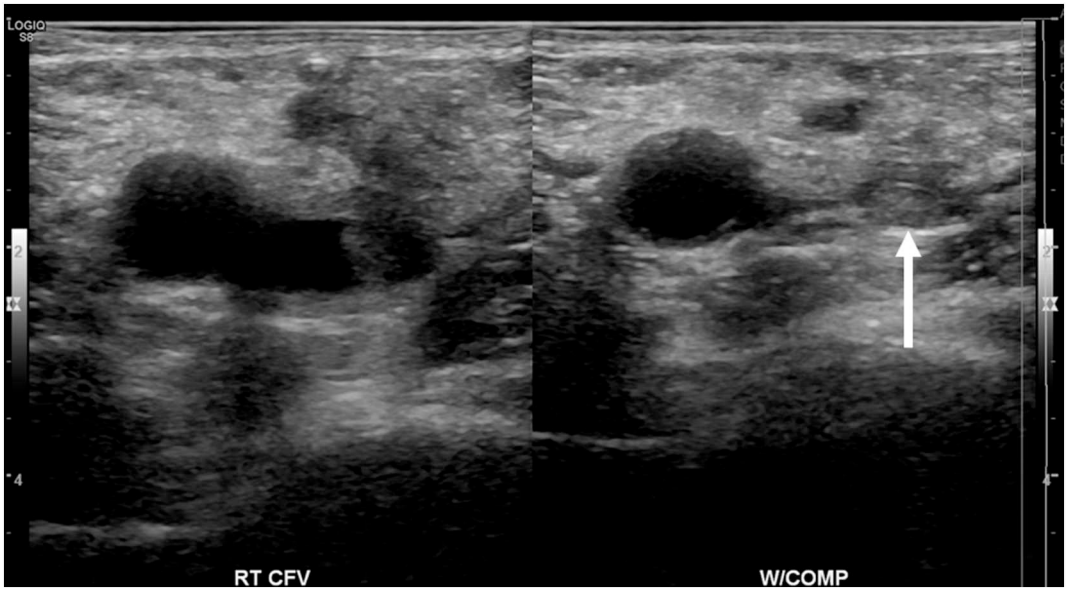

Fig. 1. Venous duplex image of right common femoral vein without compression (left image) and with compression (right image). Compression demonstrates presence of acute non-occlusive thrombus (white arrow).

https://doi.org/10.1016/j.thromres.2020.05.015
Received 1 May 2020; Received in revised form 8 May 2020; Accepted 12 May 2020
Available online 14 May 2020
0049-3848/

Table 1
Laboratory testing on initial admission and subsequent admission with complaint of right leg swelling and pain. SARS-CoV-2 Infection and Respiratory Viral Panel confirmed via Polymerase Chain Reaction (PCR) testing. Respiratory Viral Panel tests for common respiratory pathogens including non-COVID-19 coronavirus, parainfluenza, human metapneumovirus, mycoplasma pneumoniae and respiratory syncytial virus.

Laboratory testing (Normal Range)	Initial admission	Subsequent admission
D-Dimer (0.00–0.50 μg/mL)	1.73 μg/mL	8.89 μg/mL
C-Reactive protein (< 0.8 mg/mL)	6.7 mg/mL	0.6 mg/mL
Lactate dehydrogenase (< 240 U/mL)	330 U/mL	393 U/mL
White cell count (4.8–10.8 k/uL)	2.7 k/uL	8.1 k/uL
Neutrophil: lymphocyte ratio	3.2	9.6
Platelets (150–400 k/uL)	79 k/uL	238 k/uL
Alanine aminotransferase (< 40 U/L)	19 U/L	53 U/L
Aspartate aminotransferase (< 50 U/L)	43 U/L	89 U/L
Creatinine (< 1.5 mg/dL)	1.10 mg/dL	1.00 mg/dL
Prothrombin time (11.8–14.8 s)	15.0 s	15.4 s
Partial prothrombin time (25.9–38.9 s)	32.3 s	32.6 s
Creatinine kinase (20–200 U/L)	115 U/L	67 U/L
Troponin T (< 0.10 ng/mL)	0.01 ng/mL	0.01 ng/mL
SAS-CoV-2 infection	Positive	Positive
Respiratory viral panel & influenza A/B	Negative	Not Performed

improved, and he was discharged on apixaban for three months.

Coagulopathies and thrombotic complications have been increasingly noted in patients with severe disease [1–10]. In one retrospective study by Klok et al., 27% of intensive care unit patients developed venous thromboembolism (VTE) [11]. Markers of thrombosis, such as elevation of D-dimer have been reported to correlate with disease severity, development of acute respiratory distress syndrome and mortality [12–17].

Despite significant virulence and mortality associated with COVID-19 infection, 70–81% of patients undergo a mild course and require neither intensive care unit admission nor mechanical ventilation [18,19]. Many of these patients are being treated on the general medical floors, and this case illustrates the importance of maintaining a high index of suspicion for thrombosis even in mild COVID-19 cases. Our patient required no supplemental oxygen, received standard DVT prophylaxis and had only a mild elevation of D-dimer on initial admission, but still subsequently developed a debilitating thrombosis. Given significant morbidity and mortality associated with VTE and tangible worldwide prevalence of COVID-19 infections, physicians should be aware of thrombotic complications even in mild cases. Further study is required to demonstrate the prevalence of VTE, appropriate screening metrics and need for ongoing VTE prophylaxis even after discharge for patients with mild COVID-19 disease.

Declaration of competing interest

All authors contributed to the preparation of this manuscript. We have no conflicts of interest to disclose or any financial disclosures to report. The patient provided written consent for presentation of his case.

References

[1] F. Zhou, T. Yu, R. Du, G. Fan, Y. Liu, Z. Liu, J. Xiang, Y. Wang, B. Song, X. Gu, L. Guan, Y. Wei, H. Li, X. Wu, J. Xu, S. Tu, Y. Zhang, H. Chen, B. Cao, Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study, Lancet 395 (10229) (2020) 1054–1062.

[2] C. Lodigiani, G. Iapichino, L. Carenzo, M. Cecconi, P. Ferrazzi, T. Sebastian, N. Kucher, J.-D. Studt, C. Sacco, B. Alexia, M.T. Sandri, S. Barco, Venous and arterial thromboembolic complications in COVID-19 patients admitted to an academic hospital in Milan, Italy, Thromb. Res. 191 (2020) 9–14.

[3] K. Casey, A. Iteen, R. Nicolini, J. Auten, COVID-19 pneumonia with hemoptysis: acute segmental pulmonary emboli associated with novel coronavirus infection, Am. J. Emerg. Med. (2020), https://doi.org/10.1016/j.ajem.2020.04.011.

[4] G.B. Danzi, M. Loffi, G. Galeazzi, E. Gherbesi, Acute pulmonary embolism and COVID-19 pneumonia: a random association? Eur. Heart J. 41 (19) (2020) 1858.

[5] L. Spiezia, A. Boscolo, F. Poletto, L. Cerruti, I. Tiberio, E. Campello, P. Navalesi, P. Simioni, COVID-19-related severe hypercoagulability in patients admitted to intensive care unit for acute respiratory failure, Thromb. Haemost. (2020), https://doi.org/10.1055/s-0040-1710018.

[6] J.M. Connors, J.H. Levy, COVID-19 and its implications for thrombosis and anticoagulation, Blood (2020), https://doi.org/10.1182/blood.2020006000.

[7] S. Cui, S. Chen, X. Li, S. Liu, F. Wang, Prevalence of venous thromboembolism in patients with severe novel coronavirus pneumonia, J. Thromb. Haemost. n/a(n/a).

[8] J.-F. Llitjos, M. Leclerc, C. Chochois, J.-M. Monsallier, M. Ramakers, M. Auvray, K. Merouani, High incidence of venous thromboembolic events in anticoagulated severe COVID-19 patients, J. Thromb. Haemost. n/a(n/a).

[9] J. Thachil, N. Tang, S. Gando, A. Falanga, M. Cattaneo, M. Levi, C. Clark, T. Iba, ISTH interim guidance on recognition and management of coagulopathy in COVID-19, J. Thromb. Haemost. n/a(n/a).

[10] R. Bellosta, L. Luzzani, G. Natalini, M.A. Pegorer, L. Attisani, L.G. Cossu, C. Ferrandina, A. Fossati, E. Conti, R.L. Bush, G. Piffaretti, Acute limb ischemia in patients with COVID-19 pneumonia, J. Vasc. Surg. S0741–5214 (20) (2020) 31080–31086.

[11] F.A. Klok, M.J.H.A. Kruip, N.J.M. van der Meer, M.S. Arbous, D.A.M.P.J. Gommers, K.M. Kant, F.H.J. Kaptein, J. van Paassen, M.A.M. Stals, M.V. Huisman, H. Endeman, Incidence of thrombotic complications in critically ill ICU patients with COVID-19, Thromb. Res. (2020), https://doi.org/10.1016/j.thromres.2020.04.013.

[12] W.-j. Guan, Z.-y. Ni, Y. Hu, W.-h. Liang, C.-q. Ou, J.-x. He, L. Liu, H. Shan, C.-l. Lei, D.S.C. Hui, B. Du, L.-j. Li, G. Zeng, K.-Y. Yuen, R.-c. Chen, C.-l. Tang, T. Wang, P.-y. Chen, J. Xiang, S.-y. Li, J.-l. Wang, Z.-j. Liang, Y.-x. Peng, L. Wei, Y. Liu, Y.-h. Hu, P. Peng, J.-m. Wang, J.-y. Liu, Z. Chen, G. Li, Z.-j. Zheng, S.-q. Qiu, J. Luo, C.-j. Ye, S.-y. Zhu, N.-s. Zhong, Clinical characteristics of coronavirus disease 2019 in China, N. Engl. J. Med. 382 (18) (2020) 1708–1720.

[13] C. Wu, X. Chen, Y. Cai, J.a. Xia, X. Zhou, S. Xu, H. Huang, L. Zhang, X. Zhou, C. Du, Y. Zhang, J. Song, S. Wang, Y. Chao, Z. Yang, J. Xu, X. Zhou, D. Chen, W. Xiong, L. Xu, F. Zhou, J. Jiang, C. Bai, J. Zheng, Y. Song, Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China, JAMA Intern. Med. (2020), https://doi.org/10.1001/jamainternmed.2020.0994.

[14] G. Lippi, E.J. Favaloro, D-dimer is associated with severity of coronavirus disease 2019: a pooled analysis, Thromb. Haemost. 120 (05) (2020) 876–878.

[15] N. Tang, D. Li, X. Wang, Z. Sun, Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia, J. Thromb. Haemost. 18 (4) (2020) 844–847.

[16] Y. Deng, W. Liu, K. Liu, Y.Y. Fang, J. Shang, L. Zhou, K. Wang, F. Leng, S. Wei, L. Chen, H.G. Liu, Clinical characteristics of fatal and recovered cases of coronavirus disease 2019 (COVID-19) in Wuhan, China: a retrospective study, Chin. Med. J. (2020).

[17] D. Wang, B. Hu, C. Hu, F. Zhu, X. Liu, J. Zhang, B. Wang, H. Xiang, Z. Cheng, Y. Xiong, Y. Zhao, Y. Li, X. Wang, Z. Peng, Clinical characteristics of 138 hospitalized patients with 2019 Novel coronavirus–infected pneumonia in Wuhan, China, JAMA 323 (11) (2020) 1061–1069.

[18] Z. Wu, J.M. McGoogan, Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention, JAMA 323 (13) (2020) 1239–1242.

[19] E. Livingston, K. Bucher, Coronavirus disease 2019 (COVID-19) in Italy, JAMA 323 (14) (2020) 1335.

Peter C. Nauka[a], Erick Oran[b], Sweta Chekuri[b,*]

[a] *Albert Einstein College of Medicine and Montefiore Medical Center, Department of Internal Medicine, Residency Training Program, Bronx, NY, USA*

[b] *Albert Einstein College of Medicine and Montefiore Medical Center, Department of Internal Medicine, Division of Hospital Medicine, Bronx, NY, USA*

E-mail address: schekuri@montefiore.org (S. Chekuri).

* Corresponding author at: Montefiore Medical Center, Moses Division, Department of Medicine, 111 East 210th Street, Bronx, NY 10467-2401, USA.