European Journal of Case Reports in Internal Medicine

How Should Concurrent Arterial and Venous Thrombosis Associated With SARS-CoV-2 Infection Be Managed?

Athina Dimosiari[1], Dimitrios Patoulias[2], Theodoros Michailidis[3], Theodoros Dimitroulas[4]

[1] Department of Emergency Medicine, General Hospital of Kozani, Kozani, Greece

[2] Second Propedeutic Department of Internal Medicine, Aristotle University of Thessaloniki, General Hospital "Hippokration", Thessaloniki, Greece

[3] Second Department of Internal Medicine, Aristotle University of Thessaloniki, General Hospital "Hippokration", Thessaloniki, Greece

[4] Fourth Department of Internal Medicine, Aristotle University of Thessaloniki, General Hospital "Hippokration", Thessaloniki, Greece

Doi: 10.12890/2022_003366 - European Journal of Case Reports in Internal Medicine - © EFIM 2022

Received: 20/04/2022
Accepted: 07/05/2022
Published: 17/05/2022

How to cite this article: Dimosiari A, Patoulias D, Michailidis T, Dimitroulas T. How should concurrent arterial and venous thrombosis associated with SARS_CoV-2 infection be managed. *EJCRIM* 2022;**9**. doi:10.12890/2022_003366.

Conflicts of Interests: The Authors declare that there are no competing interest

ABSTRACT

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the cause of coronavirus disease 2019 (COVID-19), is associated with a high incidence of thrombotic complications involving both the arterial and the venous systems. However, concurrent arterial and venous thrombosis is extremely rare. Herein, we present the case of a 75-year-old male patient with severe COVID-19 who developed bilateral renal artery thrombosis and pulmonary embolism during the disease course. To our knowledge, this is the first such case described in the literature.

KEYWORDS

COVID-19, renal artery thrombosis, pulmonary embolism

LEARNING POINTS

- SARS-CoV-2-related coagulopathy is associated with both arterial and venous thrombotic events, which increase morbidity and mortality.
- Concurrent arterial and venous thrombotic events attributed to SARS-CoV-2 are extremely rare.
- A high index of clinical suspicion is required, while further research is needed to determine the optimal type, dose and duration of anticoagulation in such cases.

INTRODUCTION

Since its initial outbreak in China, in late December 2019, coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has been a major cause of morbidity and mortality worldwide, accounting for more than 6 million deaths so far. COVID-19 is associated with a high incidence of thrombotic complications involving both the arterial and venous systems [1]. Mechanisms such as endothelial damage, complement-induced blood clotting and systemic microangiopathy are involved in the pathogenesis of thrombotic events, increasing the burden of COVID-19 for affected patients [2]. However, concurrent arterial and venous thrombosis is rare. In addition, there is no consensus on the optimal anticoagulation treatment for these patients, including type of anticoagulant, dosage and duration of treatment.

Herein, we present a case of concurrent bilateral renal artery thrombosis and pulmonary embolism in a patient with severe COVID-19.

European Journal of Case Reports in Internal Medicine

CASE DESCRIPTION

In January 2021, a 75-year-old male patient was admitted to the Emergency Department due to symptomatic SARS-CoV-2 infection after testing positive with both a rapid antigen test and a polymerase chain reaction test a week earlier. The patient complained of recurrent fever up to 38.5°C, dyspnoea during minimal exercise, chest pain, dry cough, and abdominal discomfort with two episodes of vomiting prior to admission. His medical history included arterial hypertension, and he was a former smoker.

During initial assessment, the patient was febrile, with established type 1 (hypoxemic) respiratory failure (pO2 55 mmHg, pCO2 within normal range), while the rest of his vital signs were normal. Physical examination revealed the presence of bibasilar crackles and mild sensitivity during palpation of the upper abdomen, without any signs of acute abdomen.

Initial laboratory results revealed normocytic, normochromic anaemia (Hb 13 g/dl, normal range: 14–18 g/dl; MCV 87.8 fl, normal range: 80–99 fl; and MCHC 34.9 g/dl, normal range: 32–35 g/dl), lymphopenia (absolute number 800/µl), and increased fibrinogen (404.6 mg/dl, normal range: 180–350 mg/dl), C-reactive protein (118.6 mg/l, normal value <6 mg/l) and ferritin (2019 ng/ml, normal range: 24–336 ng/ml) levels. A marked increase in D-dimer levels was also demonstrated (2615 ng/ml, normal value <500 ng/ml). A high level of red blood cells in urine (>100 per high-power field) was also seen. An initial chest radiograph established the diagnosis of SARS-CoV-2 pneumonia, demonstrating bilateral, peripherally located ground glass opacities.

The patient was placed on symptomatic treatment, inhaled and intravenous corticosteroids, inhaled beta-2 adrenergic receptor agonist, remdesivir and low-molecular weighted heparin (LMWH) at a prophylactic dose, while oxygen was supplemented with a nasal cannula. Due to the persistence of symptoms and the laboratory finding of elevated D-dimer levels, on the second day we requested computed tomography angiography (CTA) of the chest and abdomen, which revealed the presence of a concurrent bilateral, peripheral pulmonary embolism and bilateral renal artery thrombosis resulting in renal infarction (*Figs. 1 and 2*).

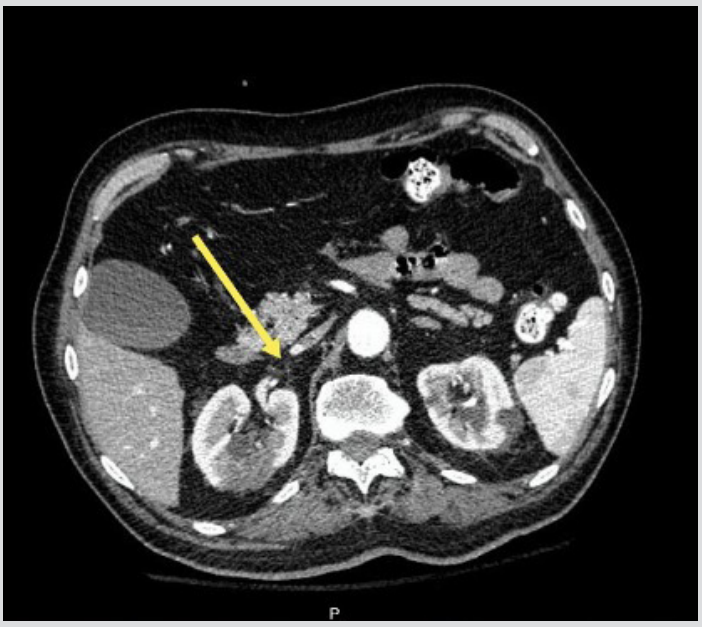

Figure 1. Bilateral renal infarction and renal artery thrombosis

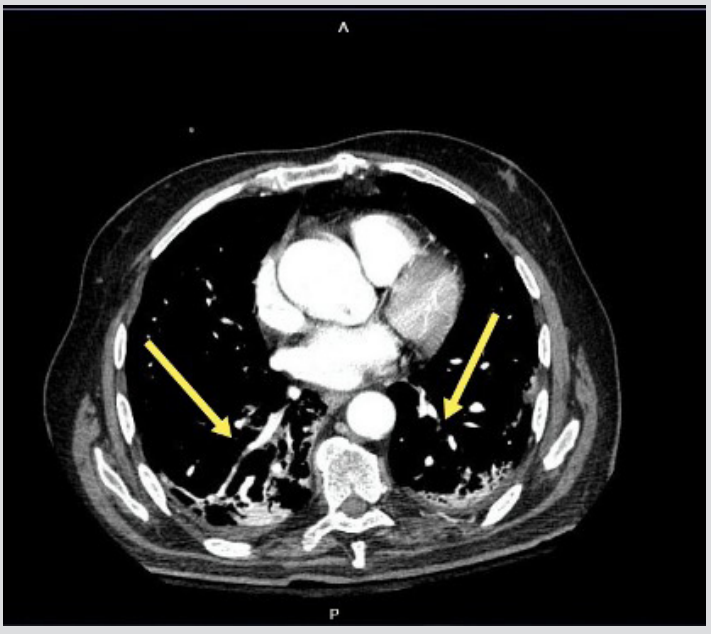

Figure 2. Bilateral, acute pulmonary embolism

A thorough investigation to exclude the main causes of inherited and acquired thrombophilia followed, which turned out negative (normal antithrombin III and protein S and C levels, negative antiphospholipid antibodies), while paroxysmal nocturnal haemoglobinuria was also excluded with multi-parametric flow cytometry. No signs of active malignancy were documented, while tumour markers were negative.

Therefore, the patient was placed on LMWH at a therapeutic dose. His disease course was uncomplicated and he was discharged 15 days later in a good general condition, with apixaban 5 mg twice daily. The patient remained asymptomatic 6 months later but was then lost to follow-up.

European Journal of Case Reports in Internal Medicine

DISCUSSION

This is the first case of concurrent renal artery thrombosis and acute pulmonary embolism in the context of SARS-CoV-2 infection described in the literature. Previously, Del Castillo-García and colleagues reported the case of a patient with severe COVID-19 who developed severe coagulopathy with multiple venous and arterial embolisms in major vessels, including bilateral pulmonary embolism, acute thrombus in the abdominal aorta, and acute thrombotic occlusion of the right iliac common artery [3].

COVID-19-induced coagulopathy is a life-threatening complication which increases the morbidity and mortality of affected patients[4]. Hyper-inflammation seems to play a critical role in the pathogenesis of such complications, although the exact pathophysiological mechanisms remain unknown. Unfortunately, despite the high incidence of thrombotic events and the close association with in-hospital mortality, therapeutic anticoagulation has not been associated with a significant effect on the risk for all-cause death [5].

In addition, there is no consensus regarding the type of selected anticoagulant, dosage or treatment duration. This remains a matter of debate according to recent evidence [6]. In the other relevant case published so far, Del Castillo-García et al. discharged their patient with therapeutic enoxaparin [3]. A forthcoming randomized controlled trial (FREEDOM COVID-19 Anticoagulation Strategy trial) will provide further, useful insights into this important issue [7].

Note that our clinical decision to treat our patient with apixaban rather than with other direct oral anticoagulants (rivaroxaban, dabigatran or edoxaban) was based on its better safety profile regarding the risk for major bleeding [8].

CONCLUSION

Herein we present the first case in the literature of concurrent bilateral renal artery thrombosis and acute pulmonary embolism in a patient with severe COVID-19. Further research is required regarding the optimal dose, type and duration of anticoagulation for patients who develop such thrombotic complications in the context of COVID-19.

REFERENCES

1. Leentjens J, van Haaps TF, Wessels PF, Schutgens REG, Middeldorp S. COVID-19-associated coagulopathy and antithrombotic agents-lessons after 1 year. *Lancet Haematol* 2021 Jul;**8**(7):e524–e533.
2. Perico L, Benigni A, Casiraghi F, Ng LFP, Renia L, Remuzzi G. Immunity, endothelial injury and complement-induced coagulopathy in COVID-19. *Nat Rev Nephrol* 2021 Jan;**17**(1):46–64.
3. Del Castillo-García S, Minguito-Carazo C, Echarte JC, Rodríguez-Santamarta M, González TB, Terroba Seara S, et al. A case report of arterial and venous thromboembolism in a patient with severe COVID-19 pneumonia. *Eur Heart J Case Rep* 2020 Nov 17;4(6):1–6.
4. 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 Apr;**18**(4):844–847.
5. Klok FA, Kruip MJHA, van der Meer NJM, Arbous MS, Gommers D, Kant KM, et al. Confirmation of the high cumulative incidence of thrombotic complications in critically ill ICU patients with COVID-19: an updated analysis. *Thromb Res* 2020 Jul;**191**:148–150.
6. Rizk JG, Gupta A, Lazo JG Jr, Sardar P, Henry BM, Lavie CJ, et al. To anticoagulate or not to anticoagulate in COVID-19: lessons after 2 years. *Semin Thromb Hemost* 2022 Apr 25. doi: 10.1055/s-0042-1744302. Epub ahead of print.
7. Farkouh ME, Stone GW, Lala A, Bagiella E, Moreno PR, Nadkarni GN, et al. Anticoagulation in patients with COVID-19: *JACC Review Topic of the Week. J Am Coll Cardiol* 2022 Mar 8;**79**(9):917–928.
8. Li G, Lip GYH, Holbrook A, Chang Y, Larsen TB, Sun X, et al. Direct comparative effectiveness and safety between non-vitamin K antagonist oral anticoagulants for stroke prevention in nonvalvular atrial fibrillation: a systematic review and meta-analysis of observational studies. *Eur J Epidemiol* 2019 Feb;**34**(2):173–190.