

# PNEUMONIA COVID-19 NON-SEVERE DENGAN KOMPLIKASI TROMBOSIS VENA DALAM

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# PNEUMONIA COVID-19 NON-SEVERE DENGAN KOMPLIKASI TROMBOSIS VENA DALAM

## Abstrak

**Pendahuluan:** Penyakit coronavirus 2019 (COVID-19) menunjukkan berbagai gejala mulai dari asimtomatik hingga mengancam nyawa. Pasien dapat datang dengan gejala infeksi saluran pernapasan yang khas maupun tidak. Pada laporan kasus ini, penulis menyampaikan pasien dengan kasus COVID-19 yang datang dengan keluhan utama bengkak di satu sisi ekstremitas bawah.

**Ilustrasi Kasus:** Seorang laki-laki, usia 48 tahun datang ke rumah sakit dengan keluhan utama nyeri dan bengkak di kaki kiri. Pasien juga mengeluhkan demam, batuk, mual disertai muntah. Pemeriksaan laboratorium menunjukkan peningkatan D-dimer. Pada ultrasonografi Doppler, didapatkan adanya trombus vena dalam di distal dan proksimal. Pemeriksaan CT angiografi pulmoner mengeksklusi emboli paru, namun pada window paru didapatkan gambaran sesuai pneumonia COVID-19. Pemeriksaan PCR swab dari naso- dan orofaring mengkonfirmasi diagnosis COVID-19. Pasien kemudian diberikan antikoagulan parenteral, dilanjutkan dengan oral saat rawat jalan. Kondisi klinis pasien membaik.

**Diskus:** Komplikasi tromboembolik telah dilaporkan sebagai penyebab tingginya kematian pada COVID-19. Aktivasi sistemik kaskade koagulasi di sirkulasi paru dan perifer dikaitkan dengan kejadian trombus yang mengancam nyawa. Pada laporan ini, pasien mengalami trombus vena dalam distal dan proksimal tanpa emboli paru yang berkaitan dengan COVID-19. Panduan yang ada menyarankan terapi dengan antikoagulan parenteral dilanjutkan extended oral anticoagulation.

**Kesimpulan:** Diagnosis dini COVID-19 dan trombus vena dalam akan meningkatkan kualitas pelayanan pasien. Antikoagulan merupakan modalitas utama dalam menangani trombus terkait COVID-19.

**Kata kunci:** COVID-19, trombus vena dalam, antikoagulan, tromboemboli vena

## NON-SEVERE COVID-19 PNEUMONIA COMPLICATED BY DEEP VEIN THROMBOSIS (DVT)

**Introduction:** Coronavirus Disease 2019 (COVID-19) displays various symptoms ranging from asymptomatic to life threatening. Patients may present with typical respiratory infection or atypical symptoms. We presented a COVID-19 case with chief complaint of unilateral leg swelling.

**Case Presentation:** A 48-year-old male was admitted to with chief complaint of cramp and swelling of the left leg. He had history of fever, cough, nausea, and vomiting. Laboratory studies showed elevated D-dimer. Doppler ultrasound shows signs of both proximal and distal deep vein thrombosis. CT pulmonary angiography excluded pulmonary embolism while the lung window image supported the diagnosis of COVID-19 pneumonia. Polymerase chain reaction (PCR) obtained from nasopharyngeal and oropharyngeal swabs confirmed COVID-19 infection. We treated the patient with parenteral anticoagulation followed by direct oral anticoagulant upon discharge. The swelling improved as well as the patient's clinical status.

**Discussion:** Thromboembolic complications has been credited as the culprit of high mortality in COVID-19. Systemic activation of coagulation in pulmonary and peripheral circulation contributed to life-threatening thrombotic complication. Our patient presented with COVID-19 associated proximal and distal DVT without pulmonary embolism. Treatment guidelines recommend the use of parenteral anticoagulants followed by extended oral anticoagulant therapy.

**Conclusion:** Prompt diagnosis of COVID-19 infection and acute DVT improves patient care. The hallmark of the management of VTE in COVID-19 patients is treatment with therapeutic dose parenteral anticoagulation followed by oral anticoagulant.

**Keywords:** COVID-19, DVT, Anticoagulant, VTE

## 5 INTRODUCTION

Coronavirus Disease 2019 (COVID-19) is caused by Severe Acute Respiratory Syndrome Corona Virus 2 (SARS CoV-2) which has spread rapidly throughout the world and was declared a global health problem by the WHO Emergency Committee in January 2020.<sup>1</sup> Symptoms of Covid-19 range from asymptomatic or mild constitutional symptoms to more severe pneumonia, sepsis and even severe acute respiratory distress syndrome (ARDS) which requires hospitalization and admission to intensive care unit (ICU).<sup>2</sup>

The clinical course of patients with COVID-19 may be complicated by coagulopathy leading to venous thromboembolism.<sup>3</sup> Current evidence revealed that COVID-19 is often complicated a significant coagulopathy, which commonly manifests as venous thromboembolism: deep vein thrombosis (DVT) and pulmonary embolism (PE).<sup>4</sup>

D-dimer levels are elevated not only in the setting of acute deep vein thrombosis (DVT) and acute pulmonary edema (PE), but also in other conditions such as infection, pregnancy, and malignancy.<sup>5</sup> However during the COVID-19 pandemic, D-dimer is commonly elevated in patients

with COVID-19.<sup>6</sup> Several recent studies suggested that patients with Covid-19 showed a condition of a hypercoagulable state. Laboratory findings show high C-reactive protein (CRP), lymphocytopenia, leukopenia, mild thrombocytopenia, prolonged PT, high fibrinogen, and high D-dimers levels in the beginning of the disease course, which in severe cases might be complicated by low fibrinogen.<sup>7</sup> Here we report a case of non-severe pneumonia COVID-19 with deep vein thrombosis as main presentation.

### CASE PRESENTATION

A 48-year-old male admitted to Kiara inpatient isolation ward with chief complaint of cramp and swelling of the left leg (Figure 1). He had history of fever, cough, nausea and vomiting 5 days before admission and have visited a general practitioner and was diagnosed with suspected typhoid fever. There were no other comorbidities. On physical examination we found the patient to be fully awake and aware, blood pressure 122/70 mmHg, heart rate 112 bpm, respiration rate 22 bpm, and temperature 37° Celsius. There were no other abnormalities except the left leg was swollen and pitting edema was present. From the laboratory studies we found: Hemoglobin level 15.3 g/dL, WBC 10,310 cells/ $\mu$ L, platelet count 636,000 cells/ $\mu$ L. Renal, liver function, and blood glucose are within normal limits. We also found elevated CRP 54.7 mg/L, Procalcitonin 0.05 ng/mL and D-dimer 20.960  $\mu$ g/L. Chest X-ray shows homogenous opacity and lung infiltrate on the base of left and right lungs.

Since the clinical, laboratory, and chest X-ray findings showed signs and symptoms suggestive of COVID-19, we performed SARS-CoV-2 PCR Swab test and the result was positive. We also performed doppler ultrasound study since the patient had the clinical pictures and Well score's pretest probability of deep vein thrombosis (DVT). CT pulmonary angiography was also requested since the d-dimer was extremely high to rule out pulmonary embolism (PE). The doppler ultrasound shows signs of deep vein thrombosis in left common femoral vein, popliteal vein through anterior tibial

vein (Figure 2). The left popliteal vein showed acute signs of DVT, hallmarked by dilation and non-compressibility (arrow) of the left popliteal vein (arrow). CT pulmonary angiography excluded pulmonary embolism while the lung window image supported the diagnosis of COVID-19 pneumonia (Figure 3).

Besides administering treatment of COVID-19 pneumonia with empirical antibiotics, symptomatic treatment, and multivitamins, we also administered parenteral anticoagulant: unfractionated heparin full dose targeted to reach aPTT of 1.5-2.5x control. After 10 days of hospitalization the swelling of the left leg improved (Figure 4). The patient then was discharged with Rivaroxaban 15 mg bid for 21 days and after that continued with Rivaroxaban 20 mg once daily.



Figure 1. Swelling and pitting edema of the left leg of the patient

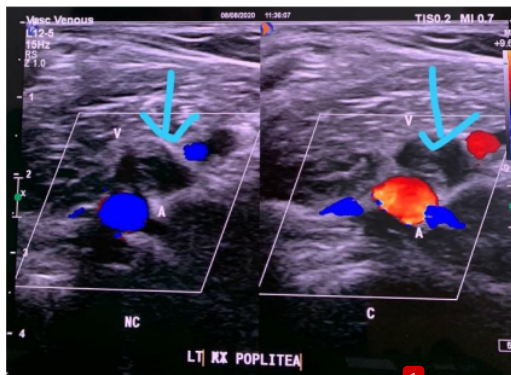


Figure 2. Doppler ultrasound image demonstrated an acute left popliteal vein DVT, hallmarked by dilation and non-compressibility (arrow) of the left popliteal vein (arrow).



Figure 4. The swelling and pitting edema of the left leg has already improved after parenteral anticoagulation followed by oral anticoagulant therapy.

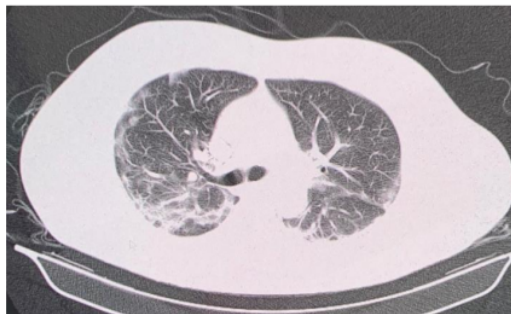


Figure 3. CT pulmonary angiography demonstrated no stenosis, aneurism, vascular malformation, or thrombus. Lung window showed ground glass opacities which supported COVID-19 pneumonia diagnosis.

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## DISCUSSION

Venous thromboembolism is a complicated disease phenomenon, with huge interplaying factors. The disease itself used to be overlooked in Asian populations due to its lower incidence compared to Western countries.<sup>8</sup> However, in medical patients, the risk of thrombosis in Asian population seems to be higher and approximately equal to its Caucasian counterparts.<sup>8</sup> The emerging COVID-19 global pandemic has opened vast array of medical research, including the ones studying thrombosis and hemostasis. Current data from case reports in this new emerging infectious disease shows that although the virus mainly targets the respiratory systems, activation of coagulation leading to coagulopathy is one of the culprit leading to high mortality in COVID-19.<sup>9</sup> Another study by Helms, et al<sup>10</sup> showed that most COVID-19 deaths are associated with thrombosis.

In this case report, our patient presented with unilateral leg swelling. The respiratory symptoms itself were not significant and the patient had continued his treatment on out-patient basis before admission. More frequently, patients with COVID-19 come to the hospital without established venous thromboembolism, although the risk of thrombosis

has already elevated in the majority of the patients.<sup>11</sup> Interim Guidelines by The International Society on Thrombosis and Hemostasis suggests that assessment of coagulation parameters should be done at patient admission.<sup>11</sup> The guideline stratifies COVID-19 patients to high-risk and low-risk of thromboembolism, and provides guidance on prophylactic anticoagulation for each group.<sup>11</sup> Other review by Carfora, et al<sup>12</sup> stratifies the anticoagulation strategy and dosing according to COVID-19 severity. However, the aforementioned publications do not provide guidance on the treatment of established venous thromboembolism.

We established confirmed COVID-19 case from the positive result of polymerase chain reaction (PCR) obtained from nasopharyngeal and oropharyngeal swabs. Prompt lower extremity vascular ultrasonography played an important role in deciding which imaging modality should be requested as the next step. Had the ultrasound not demonstrated any filling defect or compression abnormalities, a non-contrast pulmonary CT-scan would be ordered thus providing no additional diagnostic value in ruling out pulmonary embolism. The sonographic findings of acute popliteal DVT warned us to proceed with contrast-enhanced CT pulmonary angiography, which not only confirmed ground glass opacities in the lung window, but also provided a good image of the pulmonary arteries to rule out acute pulmonary embolism.

The diagnosis approach of DVT in this patient follows the clinical decision rule as described by Dronkers, et al.<sup>13</sup> High probability of DVT on admission, followed by positive compression ultrasound confirms the diagnosis of DVT. Elevated D-dimer itself can occur in COVID-19 infection without established thromboembolism. Hence, clinical probability scoring system and ultrasound play an important role in diagnosing DVT in our case.

In acute established thromboembolism, the anticoagulant treatment should be initiated promptly with therapeutic dose. Either low-molecular weight heparin (LMWH) or unfractionated heparin (UFH) can be used. Some guidelines, such as the ISTH guideline recommends LMWH while other guidelines recommend either one of them.<sup>11</sup> While LMWH provides simplicity and lower risk of patient contact, UFH gives the clinicians plenty of room for dosage adjustment even in severe renal failure. In our patient, we used UFH with dose titration to achieve the target aPTT level of 1,5-2,5 times control. We administered UFH as suggested by the review by Hajra, et al.<sup>3</sup> Parenteral anticoagulation is chosen due to its minimal drug to drug interactions with antivirals used in treating COVID-19.<sup>14</sup>

After hospital admission, we continued the anticoagulation with a direct oral anticoagulant (DOAC). Therapy with DOAC should be continued and monitored according to patient's symptoms and sonographic findings. Since this patient had both distal (anterior tibial) and proximal (common femoral and popliteal) DVT, the duration of oral anticoagulation should be the longer one, which is 3 months, as for proximal DVT.<sup>4</sup>

## CONCLUSION

Patients with COVID-19 may present with various sign and symptoms, sometimes mimicking other distinct entity, such as unilateral leg swelling. Prompt diagnosis of COVID-19 infection and acute DVT would improve patient care since the treating physician would be aware of this infectious disease and its dire thrombotic complications. Treatment with therapeutic dose parenteral anticoagulation followed by oral anticoagulant is the hallmark of the management of VTE in COVID-19 patients.

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