



POST-COVID-19 RECURRENT LOWER LIMB ISCHEMIA IN HEALTHY YOUNG PATIENT

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Background: Although SARS-CoV-2 infection is primarily a respiratory illness, complications such as arterial and venous thromboembolism have been reported during acute infection and in the period after its resolution.

Methods: We report the case of a 33-year-old male, previously healthy patient with acute recurrent unilateral arterial thrombosis of the leg occurring one month after a mild Covid-19 infection.

Results: The patient has recently been diagnosed with essential hypertension and did not have other known risk factors for arterial thrombosis. He presented to the Emergency Department with a pale left foot and absent dorsal pedal pulse and after confirmed arterial occlusion by Doppler ultrasound, he underwent urgent thromboembolectomy. The following day a computed tomography angiogram showed recurrent thrombosis of the superficial femoral artery which was then resolved in an Angio-suite by balloon dilatation. Three months later he experienced another occlusion of the left superficial femoral artery based on pronounced neointimal hyperplasia and again underwent endarterectomy with patch plastic.

Conclusion: SARS-Cov-2 infection should be considered a risk factor in the development of both arterial and venous thrombosis during the acute phase and in the post-infective period.

Keywords: COVID-19, SARS-COV-2, ARTERIAL THROMBOSIS, ULTRASOUND, LOWER LIMB, ACUTE ISCHEMIA

CASE REPORT

A 33-year-old male patient presented to the Emergency Department because of worsening left leg pain and numbness of the toes that started 4 days earlier. Physical examination revealed a cold pale left foot and lack of dorsal pedal pulse. Laboratory analysis showed only slightly elevated fibrinogen levels (4.8 g/L, reference range 1.8-3.5 g/L) and other parameters, including D-dimer levels, were normal. His past medical history

included essential hypertension discovered recently and Covid-19 infection with mild symptoms a month prior. His regular test for SARS-Cov-2 upon arrival and PCR test were negative. A Colour Doppler ultrasonography (using LOGIQ S8, Medical Systems, Wisconsin, USA) was performed and demonstrated biphasic signals in the common femoral, superficial femoral (SFA), and popliteal artery. Doppler signal was absent in the posterior and anterior tibial artery proving acute occlusion. After the consultation with a vascular surgeon, the patient underwent an emergency operation where a 5 cm long thrombus was evacuated from the SFA using a Fogarty catheter with subsequent complete recanalization of the lumen. Early postoperative CT that was done the following day revealed a recurrent parietal thrombus in the proximal superficial femoral artery (0,3 cm in length) and another one distally (1,4 cm in length) that sub-occluded the lumen (Figures 1 and 2). The interventional radio-

logist decided to perform an urgent endovascular treatment in the Angio-suite. After a pigtail catheter insertion in the abdominal aorta, angiography confirmed sub-occlusion of the middle portion of the left SFA (Figure 3) and normal flow in the popliteal artery and arteries of the lower leg. After the crossover, a balloon was placed and inflated in the superficial femoral artery in the sub-occluded lumen (dimensions 6 x 40 mm). The patient was given an intra-arterial injection of 5000 i.u. of heparin. Control angiogram showed complete recanalization (Figure 4). The patient was discharged from the hospital the following day with palpable pulsations of the SFA and distal arteries of the left leg without limitations of physical activity and underwent oral anticoagulant therapy.

Two months after, the patient underwent a control Doppler ultrasound which revealed significant stenosis of the middle portion of the left SFA with the slower flow in the distal arteries of the leg.



Figure 1.
CT angiogram showing acute thrombosis of the left superficial femoral artery.

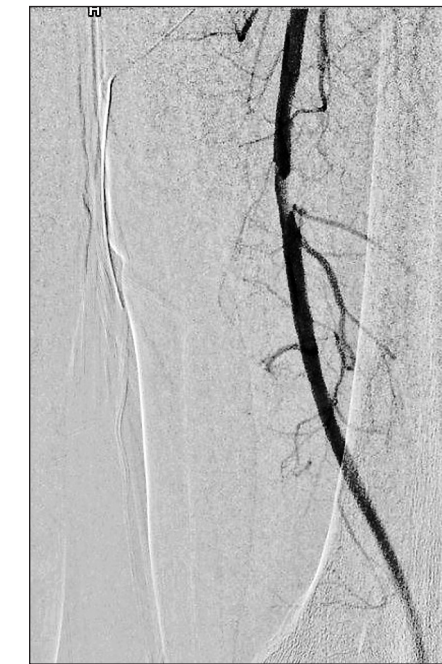


Figure 3.
Angiogram confirming recurrent thrombosis of the SFA.



Figure 2.
CT angiogram reconstruction.



Figure 4.
Angiogram performed after balloon dilatation and restitution of the lumen of the SFA.

Three weeks later, he came to the ED because of intermittent claudication of the left leg. An urgent CT-angiogram showed an occlusion of the middle portion of the left SFA (12 cm in length). The vascular surgeon indicated an urgent operation after the pronounced

neointimal hyperplasia was detected. He performed an endarterectomy with patch plastic on the left SFA. After the satisfying postoperative recovery, the patient underwent oral anticoagulant and antithrombotic therapy. The patient was referred to additional laboratory tests

to estimate his risk of thromboembolic events for recurrent thrombosis. Protective protein C and S levels were higher (1.50, 1.30 respectively - reference range 0.70-1.40), D-dimer levels were mildly elevated 1.79 mg/L (reference <0.50), cholesterol levels were 6.4 mmol/L (reference <5.0), triglyceride levels were 3.1 mmol/L (reference <1.7) and other laboratory results were unremarkable. Molecular analysis of prothrombotic gene variants showed no mutations of the coagulation factors V Leiden (FVL), FVR II, Methylenetetrahydrofolate reductase (MTHFR), and PAI-1. Only the ACE deletion/deletion (D/D) genotype was detected.

DISCUSSION

The viral infection caused by the novel SARS-Cov-2 virus was initially considered a respiratory disease causing a wide range of symptoms from mild upper respiratory tract illness to severe respiratory insufficiency (1). Various comorbidities contribute to a more severe clinical manifestation of the disease such as arterial hypertension, history of coronary artery disease, active cancer, atrial fibrillation, and chronic kidney disease (2). Recent studies, generally based on hospitalized patients in ICU and oxygen support, showed a high incidence of venous thromboembolism as a complication of this infection (3). Further investigations revealed that arterial thromboembolic complications, heart stroke, acute coronary syndrome, and acute limb ischemia are likely to occur in addition to venous thromboembolism (4, 5).

Newest reports discovered that peculiar gene polymorphisms contribute to the severe clinical presentation of the Covid-19 infection. Significantly higher frequency of PAIL1, PIA2 allele, β Fbg, ITGB3, FV, FXIII, and ACE I/D was among Covid-19 patients compared to non-severe Covid-19 patients (6). Another study showed a significantly higher prevalence (85%) of ACE deletion/deletion polymorphism in severe Covid-19 patients with only 10% of the ACE I/D genotype where these patients were not under the significant risk factors for thromboembolic events (7). This case report describes arterial occlusion

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as a complication of the SARS-Cov-2 infection in a healthy young patient. The SARS-Cov-2 virus induces a hypercoagulable state and previous studies reported acute arterial and venous thrombosis during the hospital stay, with a higher incidence in mechanically ventilated patients (3, 5).

Older age, history of coronary artery disease, admittance to ICU, and baseline values of serum D-dimer levels were registered as predictive factors for arterial and venous thromboembolism (4). Our patient did not fit into those categories, nor did he have comorbidities besides recently discovered essential hypertension.

Many case reports presented thromboembolic events as the only manifestation of acute SARS-Cov-2 infection (8, 9). However, there have been some studies about the coincidence of these complications in the post-three-week covid period after the acute infection (9). The studies proved that venous thromboembolism most often occurs in the first week after testing positive for SARS-Cov-2, especially in older patients, with a steady decrease in incidence during the following six weeks (10).

TEACHING POINT

Regardless of the severity of Covid-19 infection, this infection should be considered a relevant risk factor for thrombosis in the post-Covid period. Since there are only sporadic cases of arterial thromboembolism in this period further studies are needed to elucidate this issue and distinguish which patients have a higher chance of acute arterial thrombosis after SARS-Cov-2 infection (11). Gene polymorphisms can also contribute to severe post-Covid complications even after mild infection.

Authors contributions:

Sara Sablić: main idea, writing the case report
Maja Marinović Guić: writing the abstract and discussion
Ivan Kraljević: preparation of figures
Sanja Lovrić Kojundžić: writing the discussion.

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Sažetak

PONAVLJAJUĆA ISHEMIJA NOGE U ZDRAVOG MLADOG PACIJENTA NAKON PREBOLJELE COVID-19 INFEKCIJE

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Uvod: Iako je SARS-CoV-2 infekcija primarno respiratorna bolest, u literaturi su opisivane arterijske i venske tromboembolije tijekom akutne bolesti i u razdoblju nakon preboljenja.

Metode: Prikazujemo slučaj 33-godišnjeg prethodno zdravog pacijenta s akutnom ponavljajućom arterijskom trombozom noge mjesec dana nakon preboljenja blagog oblika Covid-19 infekcije.

Rezultati: Pacijentu je nedavno dijagnosticirana esencijalna hipertenzija te nije imao druge poznate rizične čimbenike za arterijsku trombozu. Javio se na Hitni prijem sa bljedim lijevim stopalom uz odsutne pulsacije a. dorsalis pedis te mu je napravljena hitna tromboembolektomija nakon potvrde arterijske okluzije ultrazvučnim aparatom. Idući dan mu je putem kompjuterizirane tomografske angiografije potvrđena ponavljajuća tromboza površne femoralne arterije koja je uspješno riješena balonskom dilatacijom u Angio sali. Nakon tri mjeseca ponovno se javlja sa simptomima okluzije lijeve površne femoralne arterije uzrokovane hiperplazijom neointime te je ponovno podvrgnut endarterektomiji sa postavljanjem grafta.

Zaključak: SARS-CoV-2 infekcija bi se trebala smatrati rizičnim čimbenikom u razvoju arterijskih i venskih tromboza tijekom akutne faze bolesti, ali i u post-infektivnom razdoblju

Ključne riječi: COVID-19, SARS-COV-2, ARTERIJSKA TROMBOZA, ULTRAZVUK, DONJI UDOVI, AKUTNA ISHEMIJA

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