Case Report

Aortic floating thrombi with lower limb ischemia and renal infarct in COVID-19: A remote thromboembolic complication

COVİD-19'da alt ekstemite iskemisi ve renal enfarkta neden olan aortik serbest trombüsler: Geç tromboembolik komplikasyon

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Summary– As the COVID-19 pandemic continues, its novel complications are being increasingly recognized, and new mechanisms of the disease are being unraveled. Aortic free-floating thrombus is exceptionally rare, and prompt diagnosis is vital to alleviate its detrimental end organ effects. We present a patient who was previously discharged owing to COVID-19 pneumonia, admitted with acute onset of lower limb pain, and was diagnosed with aortic free-floating thrombus ended up with embolic events. Clinicians should be aware of COVID-19-related thromboembolic complications, and close monitoring of patients with risk factors is vital for a timely and accurate diagnosis and management.

Özet– Covid-19 salgını devam ederken, farklı komplikasyonları giderek daha fazla fark edilmekte ve hastalığın yeni mekanizmaları anlaşılmaktadır. Aortik serbest yüzen trombüs son derece nadirdir ve hızlı tanı, olası uç organ etkilerini hafifletmek için hayati önem taşır. Bu vaka sunumunda, daha önce Covid-19 pnömonisi nedeniyle taburcu edilen ve akut başlangıçlı alt ekstremite ağrısı ile başvuran, periferal emboli ve renal enfarkt ile sonuçlanan aortik serbest trombüs tanısı alan bir hastayı tartışıyoruz. Klinisyenlerin, Covid-19 ile ilişkili tromboembolik komplikasyonların farkında olması ve risk faktörleri olan hastaların yakın takibi, zamanında ve doğru teşhis ile yönetim için hayati önem taşımaktadır.

As the COVID-19 pandemic continues, its novel complications are being increasingly recognized, and new mechanisms of the disease are being unraveled. Various mechanisms are hypothesized, such as binding of the virus to ACE receptors, cytokine storm, which may activate thrombotic pathways, vasculitis/direct endothelial damage, and immobility/hospitalization related stasis. Aortic free-floating thrombus has been scarcely reported as a serious complication during COVID-19 disease. We present a patient who was previously discharged owing to COVID-19 pneumonia, admitted with acute onset of lower limb pain, and was diagnosed with aortic free-floating thrombus ended up with embolic events. Clinicians should be aware of COVID-19-related thromboembolic complications, and close monitoring of patients with risk factors is vital for a timely and accurate diagnosis and management.

CASE REPORT

A 55-year-old male was admitted with chest pain, cough, and fever to the emergency department. He had a 17 pack-year smoking history and was on valsartan medication (80 mg) for essential hypertension without known coronary arterial disease or thrombophilia. He was febrile (39.3 °C) with SpO_2 88% in the room air. His blood pressure was normal (109/76 mm Hg) with sinus tachycardia (108 min^{-1}). Lung auscultation revealed bilateral fine crackles on the lung bases. Computed tomography (CT) scan of lungs showed bilateral patchy ground glass opacities, which were typical for COVID-19 pneumonia. No coronary calcification was evident. Polymerase chain reaction (PCR) testing confirmed the diagnosis. The initial laboratory results were as follows: lymphocyte: 787 μL^{-1} (1000-4800), thrombo-

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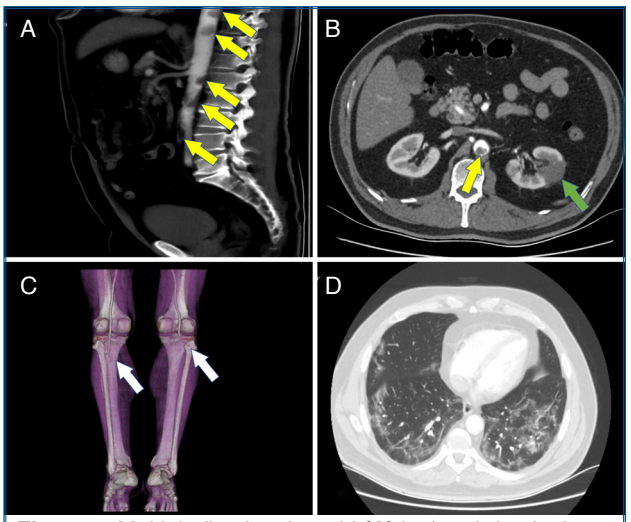

Figure 1. Multiple floating thrombi **(A)** in the abdominal aorta and right common iliac artery and **(B)** renal infarct. **(C)** No contrast filling in the left crural arteries and the right popliteal artery. **(D)** Ground-glass opacites and fibrotic changes are seen.

cyte: 177,000 μL^{-1} (150-450,000), C-reactive protein (CRP) level: 268 mg/L (<10), D-dimer: 618 ng/mL (<500), prothrombin time (PT): 12.5 s (10-13), international normalized ratio (INR): 0.9 (0.8-1.1), and activated partial thromboplastin time (aPTT): 28 s (25-36) without liver and kidney dysfunction. A mild increase in D-dimer could be indicative of coagulopathy, yet there were no signs of a thromboembolic event, which required further investigation with imaging. As he had >50% infiltration on lung CT and SpO_2 89% despite 5-L/min O_2 therapy, he was diagnosed with severe pneumonia, hospitalized, and admitted to the intensive care unit. His treatment was azithromycin (500 mg/day for 5 days), favipravir (1200 mg/day for 10 days), low-dose prednisone (32 mg/day for 5 days), and enoxaparin (0.8 mL/day for 10 days). He had no thrombocytopenia or increased D-dimer levels during hospitalization. D-dimer level at discharge was 418 ng/mL. As his symptoms were resolved and SpO_2 increased to 94% in the room air at the end of the 10^{th} day, he was discharged with 0.4 mg/day enoxaparin for 30 days as he was categorized at low-intermediate risk for thromboembolism. Four weeks after his discharge, he was admitted to our tertiary cardiovascular surgery center with an acute onset of bilateral severe lower limb and left flank pain. His anticoagulant therapy was stopped by the patient 2 weeks ago, and he was only on antihypertensive medication. The COVID-19 PCR test was negative. The laboratory results were as follows: lymphocyte: 2377 μL^{-1} (1000-4800), thrombocyte: 177,000 μL^{-1} (150-450,000), CRP: 18 mg/L (<10), D-dimer: 2566 ng/mL (<500), PT: 12.4 s (10-13), INR: 0.9 (0.8-1.1), and aPTT: 28 s (25-36). CT angiography revealed large, multiple free-floating aortic thrombi, infarct of the left kidney, and bilateral occluded crural arteries (Fig. 1). No signs of significant aortic atherosclerosis were apparent. No thrombophilia testing was ordered. He got emergency thrombectomy, and a large amount of thrombus was removed both from popliteal arteries and abdominal aorta. His distal pulses were weak at first; following 24-h intravenous heparinization (500 U/h), pulses improved. Renal infarct was managed conservatively, and his discharge therapy consisted of anticoagulation (enoxaparin in a dose of 0.8 mg/day), antiaggregant (aspirin in a dose of 300 mg/day), and pentoxifylline (600 mg). His consecutive control D-dimer levels were 1261, 873, and 688 ng/mL in the first week after surgery. Distal pulses were palpable.

Abbreviations:

aPTT	*Activated partial thromboplastin time*
CRP	*C-reactive protein*
CT	*Computed tomography*
INR	*International normalized ratio*
PCR	*Polymerase chain reaction*
PT	*Prothrombin time*

DISCUSSION

Arterial and venous thromboembolic events have been occasionally reported in COVID-19, yet the relationship between thromboembolism and COVID-19 is considered more seriously in recent literature, which is rapidly evolving.[1-3] Various mechanisms are hypothesized, such as binding of the virus to ACE receptors, cytokine storm, which may activate thrombotic pathways, vasculitis/direct endothelial damage, and immobility/hospitalization related stasis.[4] Besides, patients with older age, smoking, diabetes, and hypertension or cardiovascular diseases are prone to chronic endothelial dysfunction, which may further contribute to COVID-19-related thromboembolic complications.[5] Chronic endothelial dysfunction is the cornerstone in patients with risk factors that may be responsible for a nonadaptive response during COVID-19 infection, which plays a role in the pathogenesis of pneumonia, acute respiratory distress syndrome, or microcirculation perturbation resulting in

cardiovascular complications.[5] The activation of the coagulator pathways by the dysfunctional endothelium is indicated by D-dimer levels in severe patients, which poses a high risk for mortality and thromboembolic events.[6] Twofold increase in D-dimer levels was reported to be associated with venous thromboembolism, and a fourfold increase strongly correlated with higher mortality rates.[7] In the current national COVID-19 thromboembolism management guideline, it is recommended to extend the prophylaxis for thromboembolism up to 45 days in case of at least twofold D-dimer increase.[8] At first admission of our patient, D-dimer level was mildly elevated, yet there were no clinical signs of thromboembolism, and no further imaging was needed as no clinical deterioration was noted during hospitalization. Anticoagulation with enoxaparin (2x0.4 mL) was continued during hospitalization according to current national guideline.[8] As his discharge D-dimer level was within the normal range and there were no previous malignancy or immobile status, he was categorized as a low-risk patient, and enoxaparin in a dosage of 0.4 mg/day was prescribed for 30 days. The current national guideline recommends 14-30 days of enoxaparin, 31-39 days of rivaroxaban, or 35-42 days of betrixaban for low-risk patients. The use of aspirin is controversial for prophylaxis.[8] More than twofold increase in D-dimer, immobility, or presence of malignancy history are specified as high-risk factors for extended anticoagulation therapy, yet comorbidities such as coronary arterial disease, hypertension, or diabetes are not stated for risk assessment of thromboembolism in the current national guideline.[8]

Floating aortic thrombus is rare in COVID-19 infection, yet reported cases have been increasing gradually as the pandemic goes on. Reported risk factors for aortic thrombus are concomitant cardiovascular disease, older age (>60 years), moderate to severe pneumonia, significantly increased inflammatory, or coagulation markets at initial admission or gradual increase during hospitalization.[9-11] In our patient, the low lymphocyte count, markedly elevated CRP, and severe pneumonia findings could be suggestive of severe inflammation with cytokine storm even though he did not have significant high D-dimer values at initial presentation and during hospitalization. However, his smoking status and essential hypertension history were of reported cardiovascular risk factors, which could contribute to procoagulant status when combined with highly increased inflammatory markers and severe initial pneumonia. His premature cessation of anticoagulant therapy could be a promoter for developing aortic thrombus; however, strikingly, there are reported cases who developed aortic thrombus despite the use of anticoagulation prophylaxis.[9] There was no evident aortic atherosclerosis on the CT scan despite his smoking history. Nevertheless, there are reported cases with acute lower limb ischemia without preexisting atherosclerosis in young patients.[11]

CT angiography is essential to diagnose any aortic emergencies in suspected patients, which warrants urgent intervention. Lower extremities and renal and mesenteric arteries are the common sites for peripheral embolism in the case of aortic thrombosis.[12] We noted bilateral lower limb embolism and renal infarct in our patient. Cerebral or coronary embolism is rare and, yet, can be mortal. Although there is no consensus on the management of the aortic floating thrombus, patient status and experience of the medical center determine the therapy. Management widely varies in terms of invasiveness and effectiveness. Noninvasive therapies include anticoagulant and/or thrombolytic medicament. Interventional treatment options consist of thrombus aspiration, transfemoral thrombectomy or balloon-catheter thrombectomy, and exclusion of endovascular graft.[12] Surgical treatment options are thrombectomy, thromboendarterectomy, or aortic replacement.[13] The initial treatment for our patient was surgical thrombectomy; however, distal pulses were not fully recovered probably because of an embolic burden, which required intravenous heparinization after the surgery.

In conclusion, we presented a rare and potentially fatal complication of COVID-19 infection and its management. This case highlights that in addition to inpatient treatment strategies, patients with previous COVID-19 infection who have cardiovascular risk factors warrant closer monitorization for thromboembolism; careful patient surveillance after discharge is vital for prompt diagnosis and intervention to alleviate potential life-threatening complications.

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