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CASE REPORT

Spontaneous right coronary artery dissection in a patient with COVID-19 infection: A case report and review of the literature

COVID-19 gelişen bir hastada spontane gelişen sağ koroner arter diseksiyonu: Olgu sunumu ve literatür derlemesi

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Summary– Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is responsible for the global coronavirus disease 2019 (COVID-19) pandemic. Although SARS-CoV-2 predominantly causes viral pneumonia, it is also associated with many cardiovascular complications such as myocarditis, acute myocardial infarction, and thrombosis. Spontaneous coronary artery dissection (SCAD) is a rare form of coronary artery disease, which a few recent case reports have shown to be associated with COVID-19. The case reported here is a COVID-19 associated SCAD in a patient with no history of cardiovascular disease. The SCAD was treated with stent implantation.

Özet– Şiddetli akut solunum sendromu ile ilişkili koronavirüs (SARS-CoV-2) dünyada COVID-19 salgınından sorumludur. Her ne kadar SARS-CoV-2 öncelikle viral pnömoniden sorumlu olsa da miyokardit, akut miyokard infarktüsü ve tromboz gibi kardiyovasküler komplikasyonlarla da ilişkili olduğu gösterilmiştir. Spontan koroner arter diseksiyonu (SKAD) koroner arter hastalığının nadir bir formu olup son dönemde az sayıda olgu sunumuna göre COVID-19 ile ilişkilendirilmiştir. Bu yazımızda COVID-19 hastalığı geçirmiş kardiyovasküler öyküsü olmayan bir olguda spontane sağ koroner arter diseksiyonu sunulmuştur. SKAD stent implantasyonu ile tedavi edilmiştir.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is responsible for the global coronavirus disease 2019 (COVID-19) pandemic. Although the virus predominantly causes respiratory system infection, recent reports have shown that it is also associated with many cardiovascular complications. It has been reported that COVID-19 may cause myocarditis, type 1 and 2 acute myocardial infarction, and thrombotic complications.[1] Spontaneous coronary artery dissection (SCAD) is a rare form of coronary artery disease that has recently been associated with COVID-19 in a few case reports. The case reported here is of COVID-19 associated SCAD in a patient with no history of cardiovascular disease.

Abbreviations:

COVID-19	*Coronavirus disease 2019*
CX	*Circumflex*
LAD	*Left anterior descending*
MPI	*Myocardial perfusion imaging*
RCA	*Right coronary artery*
SARS-CoV-2	*Severe acute respiratory syndrome coronavirus 2*
SCAD	*Spontaneous coronary artery dissection*
TIMI	*Thrombolysis myocardial infarction*

CASE REPORT

A 50-year-old man was admitted to the Emergency Department with complaints of cough and fever. COVID-19 was diagnosed through polymerase chain reaction test; but as the condition of the patient was mild, he was followed up at home with favipiravir treatment. Within seven days of diagnosis, the patient experienced chest pain but did not seek medical help thinking that it was a COVID-19 symptom. In terms of cardiovascular risk factors, his background and personal and family history were unremarkable. At the end of the home isolation period, he was admitted to the cardiology clinic in another hospital. The patient had recovered from COVID-19 with a good general condition, and the physical examination was normal. However, the electrocardiogram showed

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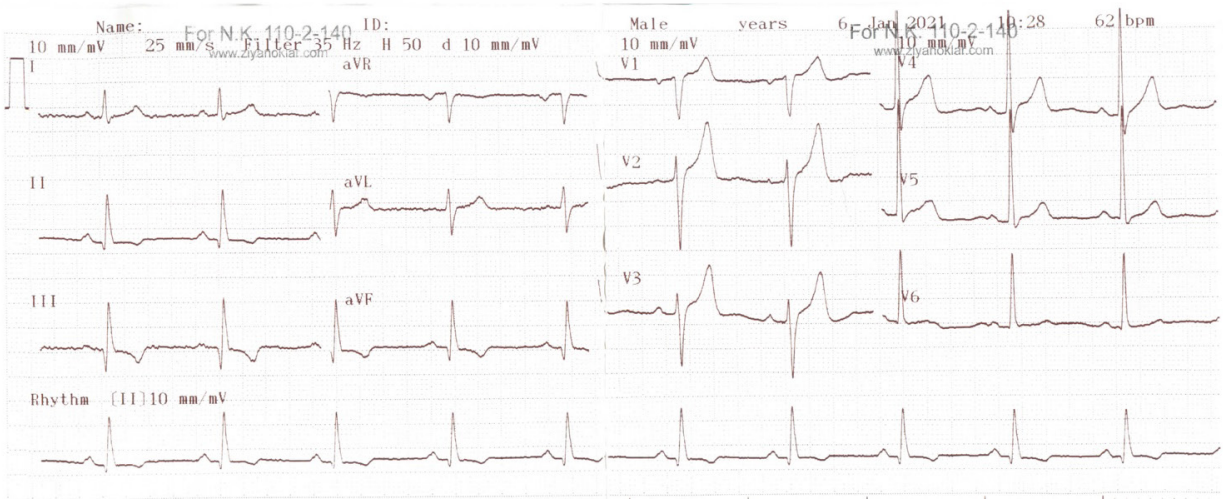

Figure 1. Twelve-lead electrocardiogram showing Q and inverted T waves in inferior leads.

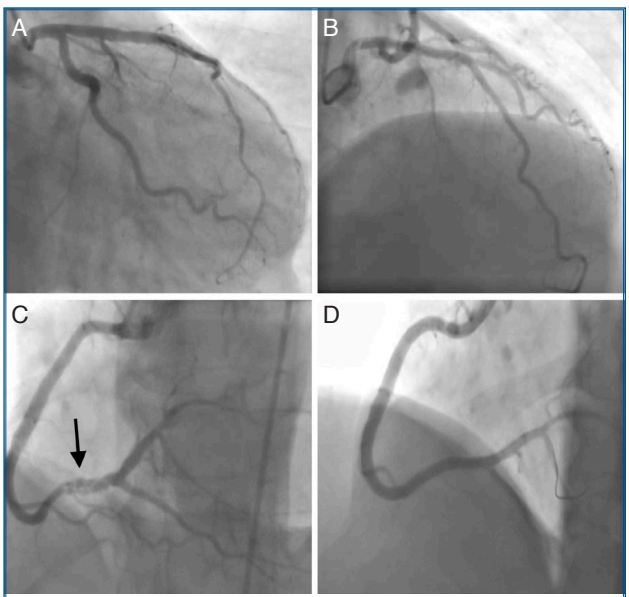

Figure 2. (A) Right anterior oblique cranial and **(B)** anteroposterior cranial images showing non-significant atherosclerotic stenosis. **(C)** The black arrow indicates dissection just before the crux of the distal right coronary artery. **(D)** The dissection was closed with a 3.5 x 28 mm bare metal stent implantation.

Q waves and T wave inversion in inferior leads (Figure 1). Echocardiography revealed 55% ejection fraction with inferior and inferoseptum wall motion abnormality (Video 1*). Myocardial perfusion imaging (MPI) was performed to rule out infarction or ischemia. MPI demonstrated ischemia in the inferior and posterior segments of the myocardium. The patient was referred to our hospital for coronary angiography. The procedure was performed via the right femoral artery after insertion of a 7-Fr sheath. The left coronary system was intubated with a 6-Fr Judkins-4 left catheter. Non-significant coronary lesions were detected in the left anterior descending (LAD) and circumflex (CX) arteries (Figure 2). The right coronary artery (RCA) was cannulated with a 6-Fr Judkins-4 right catheter. There was a long dissection in the distal RCA just before the crux with thrombolysis myocardial infarction (TIMI) 3 flow (Figure 2, Videos 2 and 3*). As there was ongoing ischemia in the corresponding area, the patient underwent coronary angioplasty. The patient was administered 300 mg acetylsalicylic acid PO, 600 mg clopidogrel PO, and 7500 U heparin IV. The right coronary artery was cannulated with 7-Fr Judkins- 4 right guiding catheter, and the dissected lesion was crossed meticulously with a workhorse catheter. After consecutive dilatation with a 2.0×20 mm balloon, dissection was closed with a 3.5×28 mm bare-metal stent (Figure 2). On the day after the procedure, the patient was discharged from the hospital with the oral treatment of 100 mg acetylsalicylic acid QD, 75 mg clopidogrel QD, 80 mg atorvastatin QD, and 50 mg metoprolol QD.

DISCUSSION

SCAD is a disruption of layers in the coronary wall, which is usually seen with the occurrence of intramural hemorrhage. Although this group of coronary lesions has been considered as coronary artery disease, they are not linked to atherosclerosis or iatrogenic trauma. SCAD can be accompanied by a dissection

Table 1. Clinical characteristics of patients with COVID-19 related SCAD

No	Authors	Published date	Origin (country)	Age, sex	Cardiovascular history	Symptoms	Predisposing factors	Timing according to COVID-19 infection	Concomitant COVID-19 complications	COVID-19 severity	Diagnosis	Vessel	Treatment	Outcome
1	Cannata et al.[3]	December 18, 2020	Great Britain	45 years, female	None	Anosmia Hypogeusia Chest pain	Unreported	8 weeks	None	Mild	STEMI	LAD	Conservative, Dual antiplatelet, Beta blocker, ACE inhibitor	Survived
2	Aparisi et al.[4]	December 21, 2020	Spain	40 years, male	None	Fever, Cough	Unreported	7 days after ECMO	Cardiogenic shock, Severe respiratory distress syndrome, Cardiac thrombus	Severe, Lung infiltration	Non-STEMI	LAD	Conservative	Survived
3	Kumar et al.[5]	May 7, 2020	USA	48 years, female	Hyperlipidemia	Chest pain	Unreported	COVID test was obtained after SCAD	Polymorphic ventricular tachycardia	Mild	STEMI	LAD	Conservative, Dual antiplatelet, Beta blocker, Amiodarone	Survived
4	Courand et al.[6]	November 12, 2020	France	55 years, male	Peripheral arterial disease	Cough, Febrile, Dyspnea, Chest pain	Unreported	48 hours after test result	None	Moderate, Crazy pavy pattern in the lung	Non-STEMI	RCA	Conservative, ASA, Statin, Beta blocker	Survived
5	Albiero and Seresini[7]	May 12, 2020	Italy	70 years, male	Smoker, Hypertension, Diabetes	Chest pain, Fever	Unreported	COVID-19 test (+) 1 day after coronary angiography	None	Mild	Non-STEMI	LAD	PCI, Clopidogrel, Bisoprolol, ASA, Atorvastatin, Metformin, Pantoprazole	Survived
6	Fernandez Gasso et al.[8]	May 7, 2020	Spain	39 years, male	None	Fever, Cough, Myalgia, Chest pain, Dyspnea	Autoimmune diseases were ruled out	Approximately 18 days	None	Severe, İntubation because of respiratory failure	STEMI	LAD, CX	Conservative, Dual antiplatelet treatment	Survived
7	Papanikolaou et al.[9]	December 23, 2020	Saudi Arabia	51 years, female	Hypertension, Smoker	Fever, Cough, Dyspnea	Unreported	3 days	None	Mild	Non-STEMI	LAD	Conservative, Dual antiplatelet, Anticoagulation, Statin	Survived
8	Kireev et al.[10]	November 27, 2020	Russia	35 years, male	Obese, Smoker	Weakness, Fever, Nasal congestion, Anosmia, Dry cough, Chest congestion	Autoimmune diseases were ruled out	Approximately 18 days	None	Mild	STEMI	RI, RCA	PCI →RI Conservative →RCA Dual antiplatelet anticoagulation	Survived
9	Yapan Emren et al. (present case)	June 1, 2021	Turkey	50 years, male	None	Cough, Fever, Chest pain (later)	None	7 days	None	Mild	STEMI	RCA	PCI, Dual antiplatelet, Atorvastatin, Metoprolol	Survived

CX: circumflex; ECMO: extra corporeal membrane oxygenation; LAD: left anterior descending; RCA: right coronary artery; RI: ramus intermedius; SCAD: spontaneous coronary artery dissection; STEMI: ST elevation myocardial infarction; Non-STEMI: non-ST segment elevation myocardial infarction.

flap, but not always.[2] Although SCAD is mostly seen in women, six of the nine patients with COVID-19 related SCAD have been reported to be men.[3-10] The age of the patients with COVID-19 ranges from 35 to 70 years, and three of the nine reported patients had no cardiovascular risk factors.[3-10] Table 1 shows the clinical characteristics of patients with COVID-19 related SCAD.

Conventional risk factors for SCAD are fibromuscular disease, pregnancy, peripartum period, sex hormones, strenuous physical exercise, vomiting, coughing anxiety, and depression. Increased levels of homocysteine related to vitamin B12 deficiency may lead to SCAD.[11] The history of the current patient showed no previous risk factors associated with SCAD. However, vitamin B12 and homocysteine levels were not examined during hospitalization. As has been shown in many inflammatory and autoimmune disorders, inflammation has an important role in the mechanism of SCAD. Recently, several patients with SCAD have been reported deemed to be associated with COVID-19. Although the pathophysiological mechanism between COVID-19 and SCAD is not currently clearly known, there are several theories. Intense inflammation and endothelial dysfunction causing sympathetic over-reactivity can lead to intimal dissection, and high-dose corticosteroid therapy may induce spontaneous rupture of the injured arterial wall.[4] Patients with mortality because of acute systemic infections have been reported to have higher macrophage, T cell, and dendritic cell counts in the coronary adventitia and intima. SARS-CoV-2 may cause activation and infiltration of T-cells in the coronary adventitia and periadventitial fat. Given the large amount of cytokines and proteases produced by T-cells, the vessel wall is vulnerable to plaque, rupture, or erosion, which can result in dissection.[12] Another suggested pathophysiological mechanism is that SARS-CoV-2 may enhance angiogenesis and proliferation of vasa vasorum. Given the leaky and fragile structure, the newly formed vasa vasorum tends to rupture, which in turn causes intramural hematoma.[13] In addition, the vasa vasorum can transit inflammatory cells to the medial and adventitial layers of the vessel, which may lead to rupture of the vasa vasorum.[14] The SARS-CoV-2 virus may use ACE receptors, which are also expressed in vascular endothelial and smooth cells, to directly invade the coronary arteries. Therefore, SARS-CoV-2 itself can induce inflammation in the vessel wall, massive death of endotheliocytes, and impair the hemostatic system and the vascular tone, which finally makes the vessel wall more vulnerable to dissection.[10]

Patients with SCAD are mainly diagnosed with myocardial infarction, and the majority have STEMI. The clinical presentation of patients with COVID-related SCAD was as follows; five of the nine patients had STEMI and four had NONSTEMI.[3-10] The most common symptom was chest pain,[2] but three patients had no chest pain. The others had symptoms uncharacteristic of coronary artery disease such as fever or cough.[3-10] The present case had the typical findings of chest pain which began within seven days of COVID-19 related symptoms. Of the previously reported patients with COVID-19 related SCAD, it was determined in the LAD (six patients), RCA (three patients), CX (one patient), and ramus intermedius (one patient). Among these, two patients had multivessel dissection.[3-10]

Coronary angiography is the current diagnostic method for the detection of coronary dissection.[2] In suspected cases, intracoronary imaging methods such as optical coherence tomography or intravascular ultrasound may be preferred to be able to delineate intimal tear and hematoma or rule out atherosclerotic plaque rupture.[15] Coronary computed tomography is promising for the determination of dissection, intimal flap, stenosis, and intramural hematoma. It should be kept in mind that before demonstrating dissection with these imaging methods, the dissected lesion must be crossed with a guidewire; and therefore, the dissection may be exacerbated during wire manipulation which may result in coronary occlusion.

According to previous reports, the majority of stable patients with SCAD were treated medically.[2] The decision for either medical or invasive treatment in the cases of myocardial infarction is a complex one. Some experts advocate revascularization if there is persistent chest pain, hemodynamic instability, ongoing ischemia or malignant arrhythmia, and high-risk anatomic features, including impaired coronary flow, multivessel proximal dissections, or left main or osteal LAD lesions.[2] Coronary artery bypass grafting should be reserved for when PCI is not successful in high-risk patients. The majority of patients with COVID-19 and SCAD (six/nine), have been successfully treated medically.[3-10] In our patient, SCAD was

treated with stent implantation as it had led to significant wall motion abnormality and ongoing ischemia.

At the beginning of the COVID-19 pandemic, based on the experience of Chinese research, thrombolytics were thought to be a favorable option for patients with both COVID-19 and STEMI. However, with the recent reports of patients with COVID-19 related SCAD, thrombolytic agents as an initial treatment for STEMI may be harmful in the presence of COVID-19. Therefore, guidelines should be revised according to new data.

Although the global COVID-19 pandemic is primarily accepted as a respiratory viral infectious disease, it may also be linked to many cardiovascular complications such as thrombosis. It is also now thought to be associated with SCAD. However, there more data is needed to be able to elaborate on the cause-and-effect relationship between COVID-19 and SCAD.

*Supplementary video files associated with this article can be found in the online version of the journal

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Keywords: COVID-19; SARS-CoV-2; cardiovascular disease; dissection

Anahtar Kelimeler: COVID-19; SARS-CoV-2; kardiyovasküler hastalık; diseksiyon