

Cardiac magnetic resonance findings in coronavirus disease 2019

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Abstract

A subgroup of COVID-19 patients with cardiac magnetic resonance imaging evidence of myocardial inflammation may exhibit subendocardial fibrosis, compatible with myocardial infarction, while epicardial coronary arteries are normal.

KEYWORDS

Cardiovascular disorders, COVID-19

1 | INTRODUCTION

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection, first reported in Wuhan, China, in December 2019, is spreading rapidly around the world. The site primarily affected by this infection is the respiratory system; however, simultaneous or even isolated cardiac involvement has been observed in some cases.¹ Coronavirus disease 2019 (COVID-19) can be diagnosed both via reverse transcription-polymerase chain reaction (RT-PCR) using pharyngeal swab specimens and via high-resolution computed tomography (CT) scans of the chest according to the recently published guidelines.²

Some investigations have furnished robust evidence of myocardial injury during the active course of COVID-19,^{3,4} with 8% of this group of patients suffering an acute myocardial insult.⁵ It is such high risks of virus-induced myocardial damage that render cardiac magnetic resonance (CMR) imaging helpful for the care of cases with suspected or confirmed COVID-19. CMR is an excellent tool for functional and morphological studies in that it confers reliable tissue characterization and differentiation between acute ischemic and nonischemic myocardial injuries.⁶

Late gadolinium enhancement (LGE) sequences are used for the detection of myocardial necrosis and fibrosis and are deemed to be of prognostic value in determining the increased risk of adverse cardiovascular events.⁷ A greater extent of fibrosis, according to LGE, is associated with a higher risk of potentially life-threatening ventricular arrhythmias.⁸

We herein present the CMR portrait of 2 definite cases of COVID-19 with evidence of extensive myocardial fibrosis.

2 | CASE 1

A 39-year-old woman presented to the emergency department with dyspnea of 1-month duration. The patient was a known case of asthma. On admission, she had a body temperature of 38°C, a blood pressure of 120/80 mm Hg, and a heart rate of 124 bpm. Physical examination revealed decreased breath sounds at lung bases with rhonchi. Her oxygen saturation level in ambient air was estimated at 89%. Given the coronavirus outbreak, nasopharyngeal and oropharyngeal swabs were immediately obtained, which indicated SARS-CoV-2 positivity.

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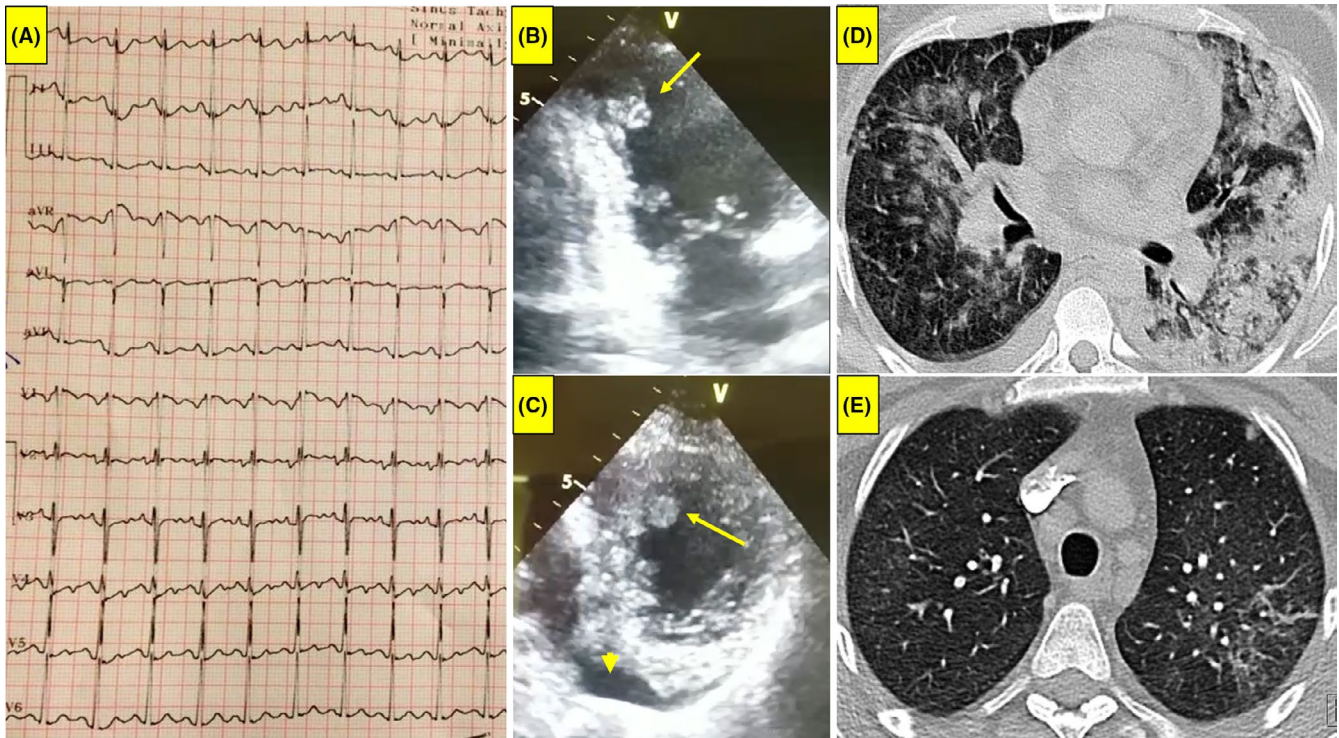


FIGURE 1 Electrocardiography, echocardiography, and chest computed tomography of CASE 1 are illustrated herein. A, Electrocardiography reveals sinus tachycardia with nonspecific ST-T wave changes. B, C, Transthoracic echocardiography shows a large mobile clot attached to the inferoapical left ventricular portion (arrow), together with mild pericardial effusion (arrowhead). D, E, Unenhanced chest computed tomography scan of the patient at initial coronavirus manifestations (D) and after 2 months (E) is depicted. Images are in the parenchymal window and from the maximum involvement level of the lung fields. D, Confluent mixed ground-glass opacity and consolidation areas in both central and peripheral distributions, associated with focal vascular dilatation; additionally, pleural and pericardial effusions are noted. E, There are a few faintly hyperdense residual opacities more in a nodular pattern with the adjacent linear densities, representing a fibrotic reaction

Panel electrocardiography (ECG) showed sinus tachycardia with nonspecific ST-T wave changes (Figure 1A). Additionally, the level of high-sensitivity troponin I (hs-TnI) was elevated (0.54 $\mu\text{g/L}$; cut point $<0.03 \mu\text{g/L}$). Transthoracic echocardiography demonstrated severe left ventricular (LV) systolic dysfunction (ejection fraction = 30%), associated with akinesia at the mid-to-apical portions of the anteroseptal and inferoseptal regions and hypokinesia in the other LV segments. There was no evidence of ventricular dilation and valvular abnormality. Also, we observed a mobile clot attached to the inferoapical LV portion, together with mild pericardial effusion (Figure 1B and C). Chest CT depicted severe multifocal consolidation and ground-glass opacity in both lungs (Figure 1D).

In the primary center, anticoagulation therapy (enoxaparin 60 mg BID, followed by apixaban 5 mg BID at discharge) and heart failure treatment (captopril 25 mg BID and spironolactone 25 mg QD, followed by carvedilol 3.25 mg BID after lung congestion reduction at discharge) were administered. Lopinavir/ritonavir was prescribed for COVID-19 treatment under the supervision of an infectious disease specialist.

Electrolytes were monitored during the admission and periodically after discharge.

Two months after discharge from the primary center, the patient was referred to our tertiary referral center for cardiac evaluation. CMR revealed myocardial edema, predominantly in the septal wall, and hyperemia (evidenced by early gadolinium enhancement sequences). Extensive patchy myocardial fibrosis with subepicardial, midwall, and subendocardial involvement in different LV segments (not in a specific vascular territory) was depicted on LGE sequences (Figure 2A-D). Pulmonary CT after 2 months showed substantial resolution in opacities despite notable cardiac involvement (Figure 1E). Also, computed tomography angiography (CTA) was performed to rule out coronary artery disease (CAD), which showed normal epicardial coronary arteries (Figure 2E-G).

Therefore, a diagnosis of active myocarditis due to SARS-CoV-2 infection with a unique involvement pattern was established. Given the patient's challenging condition, she was referred to a heart failure specialist for heart failure treatment, to be followed by another CMR 1 month later.

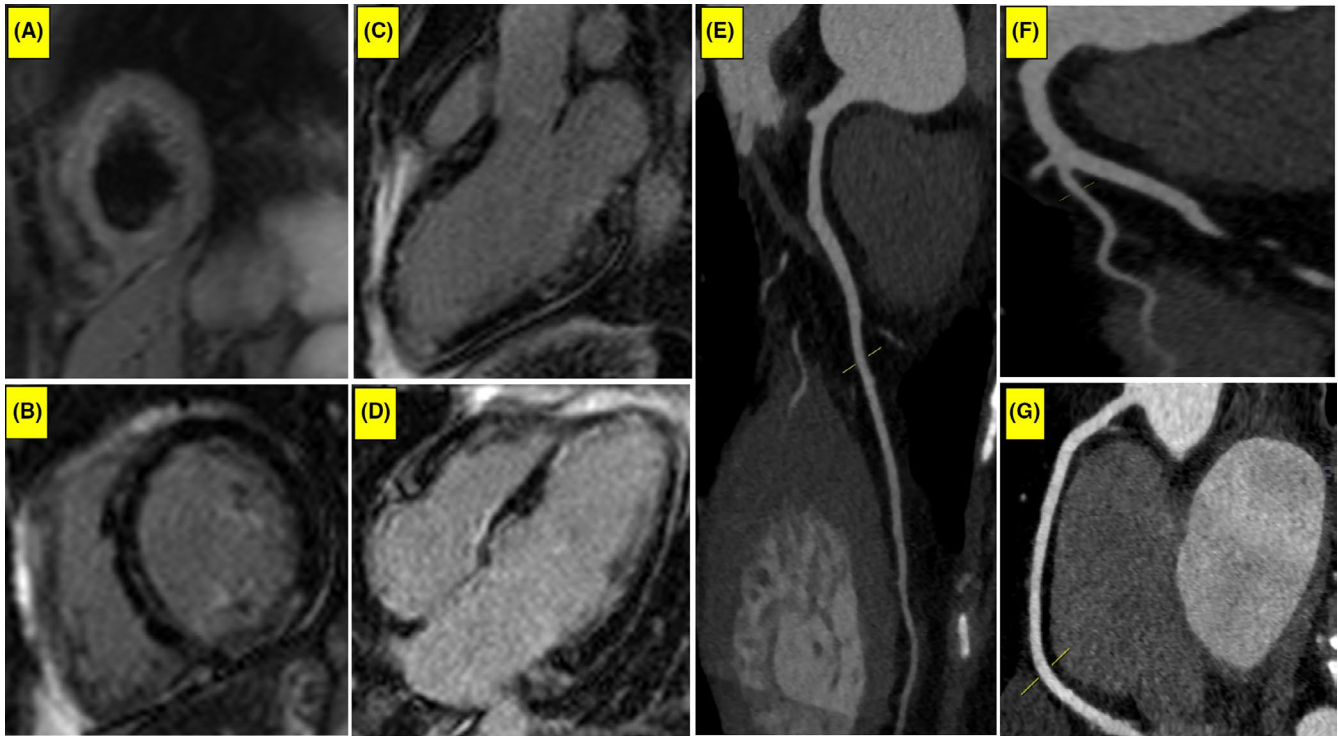


FIGURE 2 Cardiac magnetic resonance and coronary computed tomography angiography images of CASE 1 are illustrated herein. A, Short tau inversion recovery sequence in the midventricular short-axis view shows evidence of myocardial edema. B-D, Short-axis (B) 3-chamber (C) and 4-chamber (D) views depict evidence of patchy subepicardial, midwall, and subendocardial to transmural late gadolinium enhancement, representative of myocardial fibrosis. E-G, Curved multiplanar reconstruction images of normal left anterior descending (between lines in E), diagonal branch (between lines in F), and right (between lines in G) coronary arteries are depicted herein

3 | CASE 2

The patient was a 31-year-old man, who had a history of bicuspid aortic valve with severe aortic valve insufficiency, preserved cardiac function (ejection fraction = 50%-55%), and severe LV enlargement in the preceding year. He had refused to undergo valve replacement surgery.

On presentation to our center, the patient had dyspnea, atypical chest pain, a low-grade fever, and coughs. Additionally, he had a body temperature of 38°C, a blood pressure of 135/55 mm Hg, and a heart rate of 95 bpm. Physical examination was unremarkable, except for basal lung rales and 3/6 diastolic murmurs in the second intercostal space. ECG illustrated evidence of LV hypertrophy (Figure 3A).

Laboratory evaluation revealed an elevated hs-TnI level (0.32 µg/L), combined with a lymphocyte count of 1100/µL. Additionally, RT-PCR through pharyngeal swab specimens was positive.

Transthoracic echocardiography showed severe LV systolic dysfunction (ejection fraction = 10%-15%) and enlargement, severe hypokinesia in all LV segments with preserved tissue, a bicuspid aortic valve (fusion of the left and right coronary cusps) with subsequent severe aortic valve insufficiency, holodiastolic flow reversal in the descending thoracic

aorta and the abdominal aorta, and a dilated ascending aorta (Figure 3B-E). In comparison with the previous echocardiography report, documented a year earlier, a meaningful decline in the ejection fraction without a notable change in LV volume was recorded.

Chest CT depicted peripheral pulmonary ground-glass opacity and consolidation (Figure 4A). CMR was carried out for precise evaluation of the cause of the ventricular dysfunction. Similar to CASE 1, there was evidence of myocardial edema, and hyperemia along with extensive myocardial fibrosis in the subepicardial, midwall, and subendocardial regions (Figure 4B-D). CTA was performed to rule out CAD, which revealed normal epicardial coronary arteries (Figure 5).

4 | DISCUSSION

COVID-19-induced myocardial injury, with myocardial edema and fibrosis, is associated with adverse cardiac outcomes.³ Therefore, appropriate treatment crucially requires a prompt diagnosis in the early stages of the infection.

In COVID-19 cases with new-onset heart failure without known cardiovascular disease risk factors, myocarditis should be considered. Endomyocardial biopsy is not advisable in COVID-19 patients with associated myocarditis.⁴ The

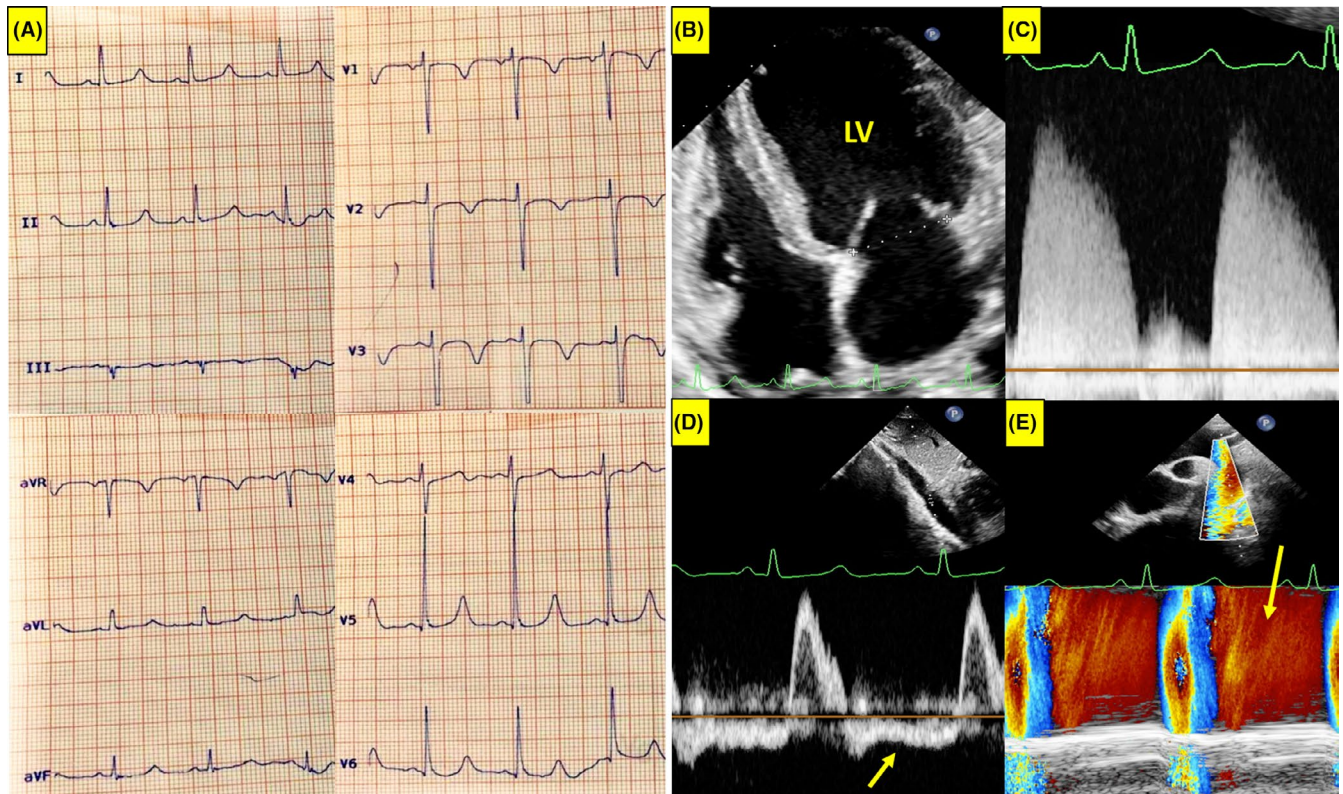


FIGURE 3 Electrocardiography, echocardiography, and chest computed tomography of CASE 2 A are illustrated herein. Electrocardiography reveals evidence of left ventricular hypertrophy. B–E, Transthoracic echocardiography in the apical 4-chamber view (B) shows severe left ventricular dilation, continuous-wave Doppler imaging (C) reveals the diastolic jet of aortic regurgitation, and pulsed-wave recording and color M-mode recording (D, E) indicate holodiastolic flow reversal within the abdominal aorta and the descending thoracic aorta, respectively (arrow)

CMR diagnosis of myocarditis (Lake Louise criteria) is on the basis of the presence of myocardial edema, hyperemia, and replacement fibrosis, with the latter evidenced by patchy LGE in affected regions. The most common locations of fibrosis are subepicardial and midmyocardial layers.⁹

In this report, we interpreted the CMR findings of 2 definite cases of COVID-19 with cardiac involvement. They both exhibited myocardial edema and hyperemia, representing underlying inflammation. In CASE 1, the myocardial edema persisted for 2 months; accordingly, we believe that cardiac involvement in SARS-CoV-2 infection can progress to a type of chronic active myocarditis or some degree of persistent myocardial edema. In a remarkable study by Puntmann et al,¹⁰ a cohort of 100 patients underwent follow-up CMR 79 days after recovery from SARS-CoV-2 infection, and cardiac involvement and active myocardial edema were scintillatingly detected in 78% and 60%, respectively, independent of preexisting conditions and the disease course. A salient finding in our patients was the concurrent involvement of all 3 myocardial layers, particularly the subendocardial stripe in the different LV segments. Subendocardial fibrosis in a specific vascular territory is a discriminating feature for differentiating acute myocarditis from myocardial infarction in that when

present, it makes CAD the most probable of all differential diagnoses. Nonetheless, in both of our cases, CAD was ruled out by CTA. According to the published investigations, COVID-19–induced myocardial injury is a result of a combination of causes.¹¹

The presence of myocardial edema and typical subepicardial/midmyocardial fibrosis in our patients may be in line with described inflammatory cascades in the COVID-19 context. The existence of subendocardial fibrosis is attributable to probable microvascular damage caused by COVID-19. We, thus, postulate that a combination of cytokine storms, inflammatory changes, and microvascular damage was culpable for ischemia with consequent acute myocardial injury in our cases.

On the other hand, in CASE 1, the presence of an LV clot in the acute phase of the disease indicated the inherent risk of clot formation, which might be due to inflammatory changes. Indeed, we may assume that LV clots can cause coronary artery embolism and the resultant myocardial infarction.¹²

In a case report, Gravinay et al¹³ described a patient with respiratory symptoms in favor of COVID-19. Despite the negative RT-PCR and chest CT results, CMR, conducted 8 days after presentation, showed subepicardial inferolateral

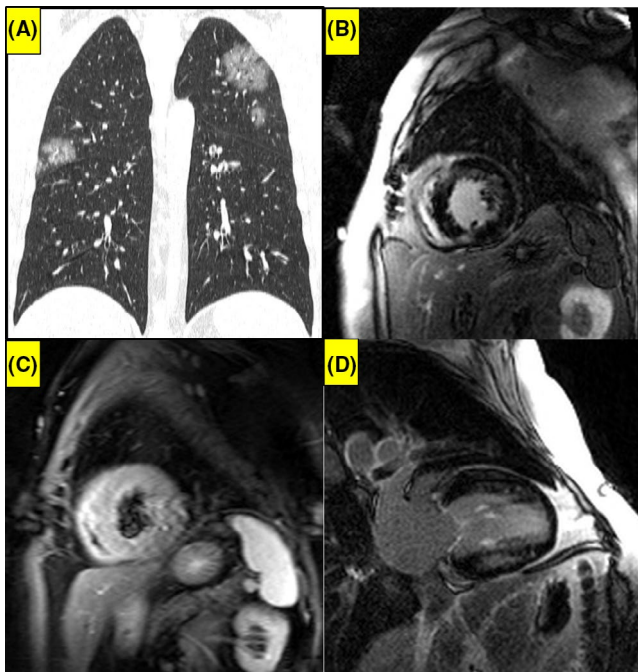


FIGURE 4 Cardiac magnetic resonance and chest computed tomography findings of CASE 2 are presented herein. A, Coronal unenhanced pulmonary computed tomography reveals segmental peripheral ground-glass opacities, which are highly suggestive of COVID-19-related pneumonia. B, Evidence of COVID-19 myocarditis is depicted in the late gadolinium enhancement sequence in the midventricular short-axis view. C, Short tau inversion recovery sequence in the midventricular short-axis view shows myocardial edema. D, Two-chamber view late gadolinium enhancement sequence demonstrates patchy myocardial fibrosis in the subepicardial and midwall regions

LV wall edema, patchy LGE, and an LV apical clot in the presence of a normal LV function. These findings are compatible with active myocarditis. Ultimately, serological tests, including immunoglobulin G and immunoglobulin M, for SARS-CoV-2 immunization, were positive. Gravinay and colleagues, thus, underscored the crucial role of CMR in the diagnostic workup of cases with suspected COVID-19.

With respect to CASE 2, we believe that the severe decline in LV systolic function in the absence of a significant rise in LV volume could not have been due to the rapid progression of valve insufficiency. The patient had no disorders such as aortic valve endocarditis that would have caused a sudden deterioration in LV systolic function. Moreover, coronary CTA, which is the preferred method to rule out CAD based on the suggested guidelines, showed no abnormality.⁴ We suspect that the diminished ejection fraction in CASE 2 may have been in consequence of an acute process such as myocarditis induced by SARS-CoV-2. This notion chimes in with the findings of some studies concluding that heart failure could follow myocarditis in the context of SARS-CoV-2 infection.^{11,12}

5 | CONCLUSIONS

SARS-CoV-2 can influence the heart through different pathophysiologic mechanisms. An unusual pattern of sub-endocardial fibrosis, typical for myocardial infarction, is recognizable in the CMR of these patients in the absence of CAD. Multimodality CMR studies may have a crucial role

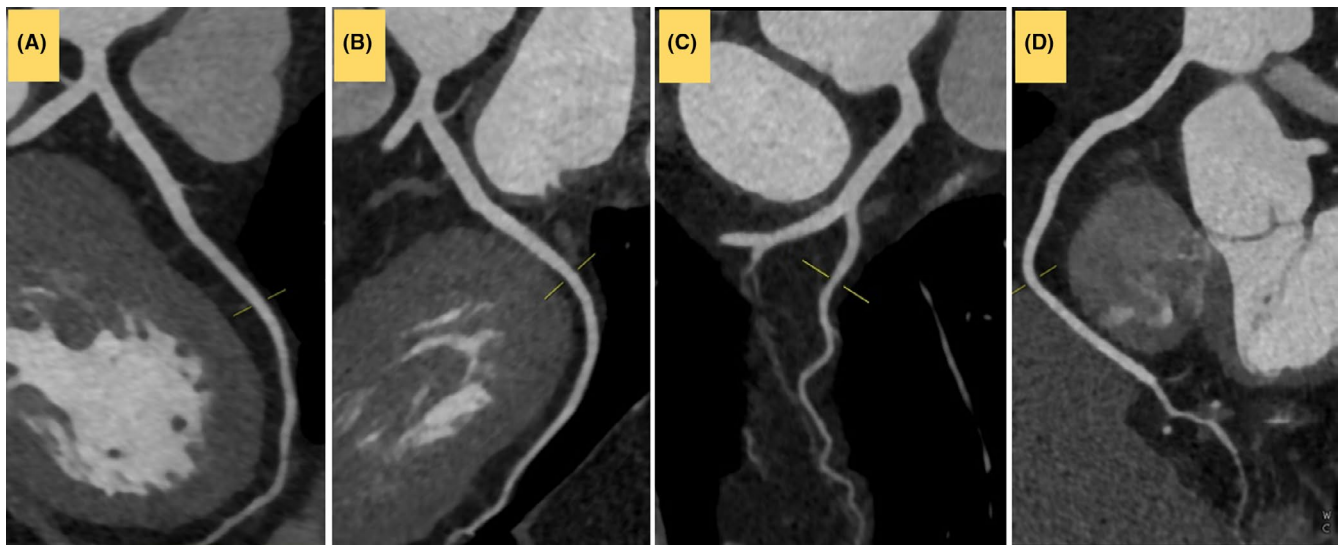


FIGURE 5 Coronary computed tomography angiography of CASE 2 is demonstrated. A-D, Curved multiplanar reconstruction images of normal left anterior descending (between lines in A), left circumflex (between lines in B), a well-developed obtuse marginal branch (between lines in C), and right (between lines in D) coronary arteries are shown

in the diagnosis of the different pathophysiological aspects of COVID-19.

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Published with written consent of the patient.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

AUTHOR CONTRIBUTIONS

All the authors: read and approved the final manuscript. Nahid Rezaeian: planned the case report, evaluated the patients, and played a major part in the writing of the manuscript. Sanaz Asadian: participated in the planning of the case report, evaluated the patients, and reviewed and discussed the manuscript. Leila Hosseini: participated in the writing and reviewing of the manuscript.

DATA AVAILABILITY STATEMENT

The datasets generated during the current report are available from the corresponding author on reasonable request.

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