Acute Coronary Syndrome and Arrhythmia Induced by SARS-CoV-2 Infection in a Patient with Non-Significant LAD Lesion. A Case Report

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ABSTRACT

Background: Coronavirus disease 2019 (COVID-19) has emerged as a pandemic and public health crisis of an unprecedented effect. Clinical studies reported an association between COVID-19 and cardiovascular disease, whereas COVID-19 itself can induce myocardial injury, arrhythmia, acute coronary syndrome, and venous thromboembolism. Case summary: A patient diagnosed via screening coronary computed tomography angiography with non-obstructive coronary artery disease was hospitalized with non-ST elevation myocardial infarction and atrial flutter during a severe respiratory infection episode with SARS-CoV-2. After recovery from the infectious episode, fractional flow reserve-guided elective percutaneous coronary intervention with drug-eluting stent was performed. Conclusions: COVID-19 intercurrence in a cardiovascular patient with nonobstructive coronary artery disease triggered coronary plaque vulnerabilization with subsequent development of an acute coronary syndrome. SARS-CoV-2 proved to be involved via direct viral tissue involvement and concomitant mechanisms derived from systemic illness in the development of a severe supraventricular arrhythmic event.

Keywords: acute coronary syndrome, COVID-19, arrhythmic event, plaque vulnerability, elective PCI

INTRODUCTION

Coronavirus disease (COVID-19), produced by a strain of coronavirus also identified as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), rapidly emerged as a global pandemic, showing disastrous unprecedented public health-related effects, while also having severe implications in social and economic activities. Amongst respiratory changes, unrestrained COVID-19 disease could also generate a cytokine storm, circumstances in which pro-inflammatory substances, such as tumor necrosis factor-α, IL-1β, or IL-6, are overproduced by the immune system, with consequential multiorgan impairment. Moreover, in
a substantial proportion of subjects, SARS-CoV-2 triggers a series of abnormalities in the coagulation cascade, which can lead to the development of thromboembolic events.2–4 Recent clinical information denotes equally the vulnerability and the consequences of COVID-19 as being strongly associated with cardiovascular disease (CVD).5–9 Besides the fact that CVD represents a mutual comorbidity reported among subjects infected with SARS-CoV-2, with a reported incidence of nearly 25%,5–7,10,11 COVID-19 seems to stimulate the progression of CV conditions such as myocardial injury, myocarditis, type 1 or type 2 myocardial infarction, severe arrhythmias, acute heart failure, cardiogenic shock, and thromboembolic events.12–14 The increased burden of inflammatory syndromes related to SARS-CoV-2 infection has been suggested to accelerate the progression of subclinical conditions or even cause de novo cardiovascular impairment.5–7

CASE PRESENTATION

A 63-year-old male patient, with history of arterial hypertension under treatment (amlodipine, valsartan), presented to the emergency department after having experienced atypical chest pain for three days. The physical and cardiovascular clinical examination exposed no abnormalities. The chest pain was treated with nonsteroidal anti-inflammatory drugs (NSAIDs).

The 12-lead electrocardiogram (ECG) performed at presentation in the emergency department identified subendocardial ischemia, with negative T waves in antero-lateral leads (V3–V6) (Figure 1). Bedside echographic examination showed no significant kinetic disturbance of the left ventricle, with preserved left ventricular ejection fraction (LVEF 50%). To exclude the possible cardiac origin of the complaints, a coronary computed tomography angiography (CCTA) was performed, which revealed no significant coronary obstruction. However, the CCTA scan showed a mixed plaque located on the left anterior descending coronary artery (LAD), with 50% luminal stenosis and not all imaging criteria fulfilled for vulnerability (Figure 2). Given the cardiovascular risk factors and associated symptoms, a

### Table 1. Timeline

<table>
<thead>
<tr>
<th>Time</th>
<th>Events</th>
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<tbody>
<tr>
<td>2019</td>
<td>• First presentation: atypical chest pain</td>
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<tr>
<td></td>
<td>• Cardiovascular risk factors: hypertension</td>
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<td></td>
<td>• MSCTA scan performed for screening: LAD 50% stenosis, mixed plaque,</td>
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<tr>
<td></td>
<td>not all vulnerability criteria fulfilled</td>
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<tr>
<td></td>
<td>• Cycle ergometer test: negative for ischemia, therefore long-term</td>
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<tr>
<td></td>
<td>imaging follow-up, antiplatelet and lipid-lowering treatment</td>
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<tr>
<td>October 2020</td>
<td>• Second presentation: typical chest pain, palpitation</td>
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<tr>
<td></td>
<td>• ECG: atrial flutter, 160 bpm → synchronized electrical cardioversion</td>
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<tr>
<td></td>
<td>• Elevated cardiac biomarkers: hs-cTnI and CK-MB</td>
</tr>
<tr>
<td></td>
<td>• Biological inflammatory syndrome: leu 17.5 G/L, CRP 273 mg/L</td>
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<tr>
<td></td>
<td>• Severe dyspnoea, persistent hypoxemia (SpO₂ 85%)</td>
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<tr>
<td></td>
<td>• Naso-pharyngeal swab resulted positive for SARS-CoV-2</td>
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<tr>
<td></td>
<td>• Due to respiratory and infectious status, invasive angiographic</td>
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<tr>
<td></td>
<td>evaluation delayed for the moment</td>
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<tr>
<td>January 2021</td>
<td>• Coronary angiography: LAD 70% stenosis</td>
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<tr>
<td></td>
<td>• FFR-guided elective PCI with DES</td>
</tr>
</tbody>
</table>

FIGURE 1. 12-lead electrocardiogram at first presentation
cycle ergometer test was performed, with negative result for ischemia. Therefore, long-term imaging follow-up and treatment with antiplatelet and lipid-lowering agents was recommended at patient discharge.

On the second presentation to the emergency department, the patient presented for typical chest pain started 2 days before, accompanied by palpitations, respiratory signs, and mild fever (38.5 °C) within the last 4 days. At the clinical examination the patient had altered status, shortness of breath, was tachypneic, with persistent hypoxemia (PaO₂ 58 mmHg) despite ventilation with a high oxygen concentration mask (6 L/min), and had crackles in both lung fields without any signs of congestion. The 12-lead ECG identified atrial flutter with a heart rate of 160 bpm and diffuse ST–T segment modifications (Figure 3). Given the symptoms and hemodynamic instability at presentation, synchronized electrical cardioversion was performed in the ER department.

Laboratory tests revealed significantly high values of high-sensitivity troponin I (upward of 11,000 pg/mL, reference range: 0.0–24.0 pg/mL) and creatine kinase MB (CK-MB) (98 U/L, reference range: 0–23 U/L). Therefore, a non-ST-elevation myocardial infarction was suspected. Moreover, a biological inflammatory syndrome was revealed, with leu: 17.5 G/L and CRP value of 273 mg/L.

Due to the systematic suspicion of COVID-19 in subjects presenting respiratory failure associated with fever, a polymerase chain reaction test was performed on a naso-pharyngeal swab, which returned positive for SARS-CoV-2. In the epidemiological and clinical circumstances stated above, invasive coronary angiography was delayed, while dual antiplatelet therapy (acetylsalicylic acid and clopidogrel), anticoagulation with LMWH, lipid-lowering agent, and a proton-pump inhibitor were immediately initiated.

After the acute respiratory distress syndrome has been treated, the patient was readmitted to cardiology in order to perform invasive angiographic reassessment and to establish the therapeutic strategy to follow. In the third admission, coronary angiography revealed a LAD coronary lesion with 70% stenosis. Fractional flow reserve (FFR)
measurements were performed guiding elective coronary angioplasty with drug-eluting stent for the LAD lesion. The patient gave informed consent allowing the publication of his data, and the institution where the patient had been admitted, approved the publication of the case.

DISCUSSIONS

Currently available clinical data report both the susceptibility and the outcomes of SARS-CoV-2 as being related with cardiovascular disease.5–9 This case further demonstrates the significant cardiovascular morbidity potentially caused by COVID-19. In this case report, the occurrence of SARS-CoV-2 in a subject with previous nonobstructive coronary artery disease led to the development of concomitant acute coronary syndrome and severe arrhythmia, therefore several issues arise.

First, a nonvulnerable coronary plaque has progressed to aggravation in spite of optimal anti-ischemic therapy. Given the intercurrence of respiratory infection with SARS-CoV-2, the hypothesis of viral implication in triggering an increase in the vulnerability of a coronary lesion, with consequent increased risk of myocardial infarction, could be taken into consideration. Therefore, patients infected with SARS-CoV-2 may present an increased risk for conversion from an asymptomatic, subclinical coronary artery disease to an unstable status, characterized by multiple vulnerable coronary plaques, as a consequence of the immunopathology associated with the viral infection.15 Although currently there is no information regarding the exact trigger responsible for plaque instability, “Kounis syndrome”, known as a myocardial infarction produced by the massive activation process of inflammation in anaphylactic conditions, could exemplify the correlation between a tremendous inflammatory trigger, coronary plaque instability, and the atherothrombotic process.16 If this hypothesis is confirmed, it could also mean that in COVID-19 patients further protective measures are needed for plaque stabilization, such as cardiovascular treatment, including antithrombotic prevention,17 and possibly therapy aiming the immunologic pathways involved in the infection.18

Second, the question arises whether the severe arrhythmia, considered as an equivalent for the cardiac stress test, developed as a result of persistent severe hypoxemia, or was the myocardial ischemia responsible for triggering the arrhythmic event? Our up-to-date understanding of the influence of SARS-CoV-2 on the development of arrhythmic events remains to progress as new records arise.5 Arrhythmic events are considered common manifestations of SARS-CoV-2, as recent records report heart palpitations as the first symptom in SARS-CoV-2 subjects after the most common fever or cough.20 Nevertheless, the precise involvement of COVID-19 in the development of cardiac arrhythmic events is unclear given that they can be initiated by myocardial injury or even systemic factors such as fever, sepsis, hypoxia, or electrolyte imbalances.13,21 A series of mechanisms could be involved in the escalation of risk for cardiac arrhythmias during SARS-CoV-2 infection. Arrhythmic events are not simply caused by the direct influence of COVID-19 infection, but rather are likely to be the outcomes of a systemic disorder.22 This could be a direct result of hypoxemia stemming from the primary involvement of lung parenchyma, myocardial inflammation, or an abnormal systemic immune response, or it could be secondary to myocardial ischemia, myocardial strain caused by pulmonary hypertension, electrolyte imbalance, intravascular volume overload, or side effects of medical therapies.

Third, from the point of view of arrhythmia management, besides the rhythm and rate control via medical therapies, another question arises. From an electrophysiological point of view, given the current global epidemiological circumstances, what would be the indications for ablation in a cardiovascular patient with a history of SARS-CoV-2 infection? And if the patient presents indication for ablation, when would the optimal timing be?

CONCLUSIONS

COVID-19 intercurrence in a cardiovascular patient with nonobstructive coronary artery disease triggered coronary plaque vulnerabilization, with subsequent development of an acute coronary syndrome. SARS-CoV-2 proved to be involved via direct viral tissue involvement and concomitant mechanisms derived from systemic illness in the development of a severe supraventricular arrhythmic event.

CONFLICT OF INTEREST

Nothing to declare.

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