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Coronary Thrombosis in a Patient with COVID-19 Who Was on Anticoagulant Therapy

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ABSTRACT

Introduction: COVID-19-related thrombotic events are associated with an increase in the risk of mortality and morbidity. Considering the research on the pathophysiology of the disease, the significance of cardiac thrombosis is being more recognized.

Case Presentation: This study aimed to present the first case report of a Left Main Coronary Artery (LMCA) thrombosis due to COVID-19 infection in a middle-aged male with a mechanical valve on anticoagulant therapy and with an International Normalized Ratio (INR) within the therapeutic range.

Conclusions: The results suggested that the therapeutic INR range may need to be higher (about 3.5) during the acute phase of COVID-19 infection to prevent thrombotic events amongst patients with COVID-19 who are on anticoagulant therapy. However, further evidence is required to determine the target range for INR in patients with COVID-19 who are on anticoagulants prior to infection.

1. Introduction

In December 2019, an outbreak of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection occurred in Wuhan, Hubei province, China and spread across China as well as around the world (1, 2). This case report aims to present a patient who developed a Left Main Coronary Artery (LMCA) thrombosis due to COVID-19 infection despite being on anticoagulant therapy and having an International Normalized Ratio (INR) within the therapeutic range.

2. Case Presentation

On 16 December 2020, a non-smoker 53-year-old man with a past medical history of diabetes mellitus, hypertension, hyperlipidemia, rheumatic degenerative valvular disease, ischemic heart disease, coronary artery bypass grafting (Saphenous Vein Graft (SVG) to the Left Anterior Descending (LAD) artery), aortic valve replacement, and mitral valve repair surgery about four years ago presented to the hospital with chest pain, nausea, vomiting, and cold sweating since three days ago. The patient declared a history of fever, cough, and diarrhea nearly two weeks ago with a positive result of a nasopharyngeal real-time polymerase chain reaction for SARS-CoV-2. However, he was treated as an outpatient and did not require hospitalization. Aspirin (80 mg daily), atorvastatin (20 mg daily), losartan (25 mg twice daily), propranolol (10 mg twice daily), warfarin (2.5 mg daily), gliclazide (80 mg three times daily), and pantoprazole (40 mg daily) were mentioned as his home medications. The results of vital signs examination revealed a blood pressure of 90/60 mmHg, tachycardia with a heart rate of 120 beats per minute, respiratory rate of 22 breaths per minute, oxygen saturation of 92%, and temperature of 37.1 ºC. On initial examination, the patient was diaphoretic with cold clammy extremities. Electrocardiogram (ECG) showed diffuse significant ST-segment depression (I, aVL, V1-V6) and 1 mm ST-segment elevation in lead aVR (Figure 1). Lab investigations demonstrated a rising trend of initial troponin-I level (first sample: 0.1, after 6 hours: 3.7, normal range: < 0.5 Mic gr/L) and CK-MB (151, normal range: < 24 U/L). The patient received aspirin, clopidogrel, weight-based intravenous heparin, high-intensity atorvastatin, and metoprolol tartrate according to the American College of Cardiology (ACC) guidelines. Emergent cardiac catheterization showed a huge thrombus in the distal part of LMCA, an ostial thrombus with TIMI I flow anterogradely

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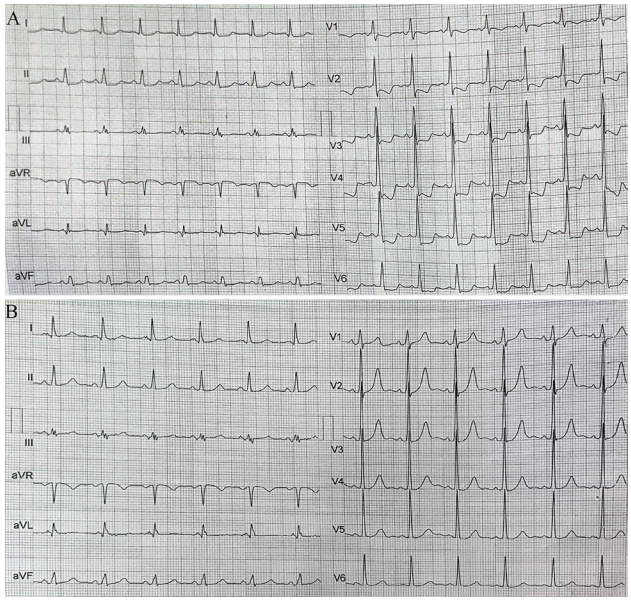


Figure 1. ECGs Series. (A) On Admission, ECG Showed Normal Sinus Rhythm with Diffuse Significant ST-Segment Depression (I, aVL, V2-V6) and 1 mm ST-segment Elevation in Lead avR. (B) Normal Sinus Rhythm without ST-segment Change Was Demonstrated in the Follow-up ECG in the Outpatient Clinic after Discharge.

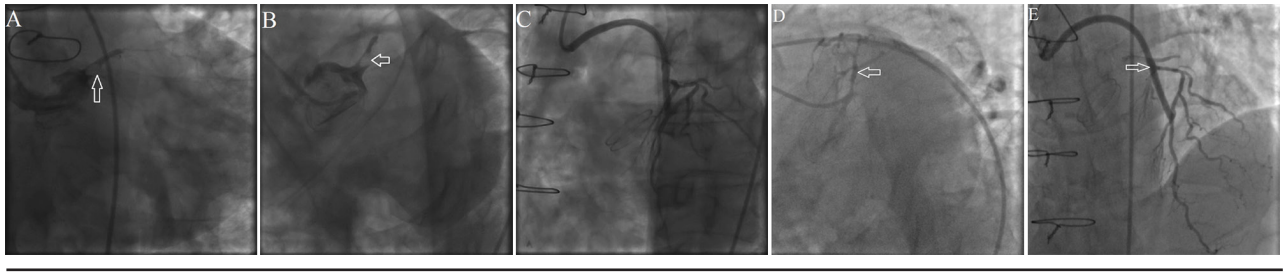
in the LAD artery (the native LAD artery and diagonal branches were well filled via SVG), an ostial thrombus with TIMI I-II flow in the Left Circumflex (LCX) artery (Obtuse Marginal (OM) branches were filled with TIMI II flow), and normal flow of the right coronary artery and posterior descending artery (Figure 2). Due to thrombotic manipulation, an intra-aortic balloon pump or stent could not be inserted. Screening for the prothrombotic state (protein C, protein S, anticardiolipin antibody, and Factor V Leiden) was negative. With a diagnosis of LMCA thrombus formation, transesophageal echocardiography was done to evaluate the embolism or vegetation originated from mechanical valves, which revealed normal biventricular size and function (left ventricular ejection fraction: 55%) without any paravalvular leakage or superimposed thrombus. Medication therapy was continued for 16 days and the second angiography showed the complete resolution of the LMCA thrombosis with an occluded LCX artery (Figure 2). Considering the patient's stable and asymptomatic condition, he was discharged on aspirin, clopidogrel, beta-blocker, angiotensin-converting enzyme inhibitor, statin, and warfarin with INR = 3.5. In the follow-up visit to the outpatient clinic about two weeks later, the patient was asymptomatic with a normal ECG (Figure 1).

The study protocol was approved by the university's Ethics Committee. In addition, written informed consent for publication of the information and images was provided by the patient.

3. Discussion

Since the onset of the COVID-19 pandemic, a growing body of evidence has shown that a substantial proportion of infected patients may have cardiovascular complications (3). There has been an increasing recognition of extra-pulmonary and cardiac-related injuries due to thrombosis in patients with COVID-19, which may be an exacerbation of a previous atherosclerotic disease and endothelial damage or a manifestation of a de novo thrombus. These cardiac involvements include myocardial infarction, in-stent thrombosis, and sudden left ventricular dysfunction (4). The exact mechanism of thrombosis formation in COVID-19 is not known yet. Elevated inflammatory cytokines are present in patients with COVID-19. Pro-inflammatory cytokines including tumor necrosis factor-alpha and Interleukin (IL)-2R, IL-6, IL-8, and IL-10 activate the coagulation cascade and inhibit fibrinolysis. A significant elevation of nonspecific inflammatory biomarkers including C-reactive protein, erythrocyte sedimentation rate, and ferritin as well as several pro-coagulant factors such as von Willebrand factor and factor VIII has also been detected in hospitalized patients with COVID-19. Although no causative connection has been established between these cytokines and COVID-19, many of these cytokines have shown a prothrombotic effect, either alone or in combination, in other settings. The presence of lupus anticoagulant in some patients also indicates the possibility of the antiphospholipid antibody syndrome as a potential contributor to thrombogenesis. In general, viral infections and sepsis both trigger coagulation via the innate immune system including activation of the tissue factor, complement systems C3a and C5a, and von Willebrand factor. Particularly, viruses can trigger the extrinsic coagulation pathway mediated by tissue factor and factor VIIa (4). In addition to COVID-19 infection, there are multiple causes for LMCA thrombus including spontaneous plaque rupture, coronary manipulation, pro-thrombotic state, blunt trauma, coronary vasospasm, coronary artery embolism arising from the aorta or native/mechanical valves, paradoxical embolism, Kawasaki's disease, and cocaine use (5). These causes were investigated

Figure 2. Coronary Arteries Angiography.



(A, B) The arrow shows a huge Left Main Coronary Artery (LMCA) thrombosis. (C) The native Left Anterior Descending (LAD) artery and diagonal branches were well filled via Saphenous Vein Graft (SVG). (D, E) The arrow showed the complete resolution of the LMCA thrombosis with the normal flow.

in the present case. The patient had no history of recent blunt trauma or cocaine use. Screening for the prothrombotic state (protein C, protein S, anticardiolipin antibody, and Factor V Leiden) was also negative. In addition, transesophageal echocardiography was performed and the findings were unremarkable for embolism and vegetation originated from mechanical valves.

Up to now, there are several reports of coronary thrombus in COVID-19 (6-10). The present case was different as he had formed a coronary thrombus while he was on anticoagulant therapy and had an INR within the therapeutic range. This suggests that the therapeutic INR range may need to be higher (about 3.5) during the acute phase of COVID-19 infection to prevent thrombotic events in patients with COVID-19 who are on anticoagulant therapy. Nonetheless, further evidence is required to determine the target range for INR in patients with COVID-19 who are on anticoagulants prior to infection.

3.1. Ethical Approval

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3.2. Informed Consent

Written informed consent forms were obtained from the patients.

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Authors' Contribution

H. B.: Conceptualization, Review & Editing, Supervision. M. H.: Software, Investigation, Data Curation, Writing - Original Draft, Visualization. F. F.: Software, Investigation, Writing - Original Draft. A. A.: Writing, Supervision. S. S.: Software, Writing - Review & Editing.

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Financial Disclosure

The authors declare that there is no conflict of interest.

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