Acute progressive arterial thrombosis after coronary artery bypass graft in a COVID-19 patient

Mahmoud Beheshti Monfared1, Hamid Ghaderi1, Zahra Ansari Aval1*, Seyedeh Adeleh Mirjafari2

1Cardiovascular Research Center, Department of Cardiovascular Surgery, Shahid Beheshti University of Medical Sciences, Tehran, Iran
2Department of Pediatrics, Ali-Asghar Children’s Hospital, Iran University of Medical Sciences, Tehran, Iran

Abstract

The longer the SARS-CoV-2 pandemic takes, the greater the prothrombotic effects of the disease, which varies from venous thromboembolic events to limb arterial thrombosis and stroke. How we deal with the effects of the COVID-19 disease, is still unclear. In this study, researchers will report the clinical presentation, outcome and management of the patient with COVID-19 after coronary artery bypass graft (CABG) surgery, which led to rapid progression of arterial thrombosis. The COVID-19 positive patient underwent emergency CABG, due to developed coronary artery disease. Despite receiving high-dose preoperative Plavix and heparin and also postoperative aspirin, the patient developed progressive thrombosis in both lower extremities 4 days after surgery. It then spread to bilateral iliac arteries, aorta, abdominal and renal artery. Femoral endarterectomy was performed two times for atheromatous plaque removal which was unsuccessful and the patient died few days later due to multi-organ failure. COVID-19 is a risk factor for arterial thrombosis with high mortality and morbidity rate. If thrombosis happens, the prognosis will be poor. Comprehensive treatments have to be started immediately after diagnosis. In patients undergoing surgery for extensive arterial thrombosis due to poor prognosis, not only surgical revascularization is needed but also thrombolysis treatments may be considered as off-label use. As the pandemic continues, new approaches and interventions may be applied.

Introduction

Although COVID-19 infection is primarily a disease of the respiratory system affecting lung parenchyma, hypercoagulable symptoms are observed in many cases, which indicates poor prognosis (1-3). This increase in coagulation can lead to arterial and venous thromboembolic events (4-7). Mortality rate among patients with ischemic limbs is usually less than 5% (8,9) and in patients with COVID-19 it is reported more than 50% (10). There are not enough studies showing the evidence of developing limb ischemia among COVID-19 positive patient who underwent surgical interventions and this may be the first report of limb ischemia after open heart surgery in a patient with COVID-19.

Case Presentation

A 55-year-old man was referred to the emergency department due to severe chest pain and was diagnosed with acute coronary syndrome (ACS). Few hours later, angiography was performed after receiving Plavix. Angiography revealed left main and three-vessel disease. Chest CT imaging was performed and featured coronavirus disease. PCR test (SARS-Cov 2 RNA test) was taken, although the result was expected to obtain 48 hours later. Despite the very high risk, the patient was a candidate for emergency open heart surgery due to the severe left main. Therefore, intra-aortic balloon pump (IABP) was installed in the right leg for the patient in the cath lab and high-dose injection of heparin was started. The patient underwent coronary artery bypass graft (CABG) surgery. The operation was successfully performed and he separated from the cardiopulmonary bypass (CPB) pump easily. He needed inotropic drugs after procedure and extubated 36 hours after surgery, although he was still dependent on inotropes and IABP. On day 4 post-op, the lower extremities pulse diminished and the patient

*Correspondence to
Zahra Ansari Aval,
Email: z.ansari@sbmu.ac.ir

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complained of pain in his right leg. IABP was removed from his right lower limb, but the patient's pain increased and his feet became cold. The pulses were lost and it was progressing gradually. Injected heparin was continued and the dose increased. As the patient underwent surgery, the use of fibrinolysis was contraindicated and could not be prescribed. The color duplex ultrasound was performed on the patient's bedside and extensive thrombosis was reported in the right lower extremity arteries. A vascular surgery consult was requested and a few hours later, the patient was transferred to the operating room. The femoral artery was explored under local anaesthesia and conscious sedation, then open thrombectomy was performed and blood clots were removed. The extremities blood flow and patient's pulse were established and he was transferred to the ICU. After a few hours, both lower limbs pulses were not palpable and the patient developed resistant acidosis. CT angiography showed arterial thrombosis in both legs. A few hours later, the patient was transferred to the operating room again. He was re-intubated due to respiratory distress and refractory acidosis. The embolectomy was performed on both lower limbs, blood flow and pulses were established and the patient was transferred to ICU. Bilateral cool extremities with pedal pulses loss happened again a few hours later. His urine output also decreased. Doppler ultrasound showed extensive thrombosis in the lower extremities which spread into the pelvic and renal arteries. The patient passed away within 36 hours of the onset of symptoms of thrombosis.

**Discussion**

COVID-19 can lead to both arterial and venous thromboembolic events (4,5). Its complications are becoming more and more known. It is recommended to consider COVID-19 disease in all patients complaining of arterial ischemia (10). The ACS and severe arrhythmia and exacerbation of heart failure were triggered with previous coronaviruses infection and influenza epidemics (11). These complications are exacerbated in COVID-19 disease. In this study patient’s ACS, manifestations may have happened due to these changes. Researches show the prevalence of heart damage in COVID-19 patients is 11%, with 16% worsening of heart condition and 14% of arrhythmia (1). Perhaps the suddenly developed ACS and patient’s instability might be happened due to COVID-19 infection, as the patient was 55 years old with no history of previous heart problem. It is probably the first reported case of acute arterial ischemia in a COVID-19 positive patient undergoing open heart surgery. So far, most of the studies discuss this issue in non-surgical patients.

In the largest study of 12630 hospitalized patients with COVID-19 infection, 49 patients showed thromboembolic events. Among this group, 37 patients (76%) were male with the mean age of 67 years (58-75 years) (10). Recent studies show increased number of deaths among COVID-19 positive patients with ischemia. Early researches reported 21%-26% mortality rate in patients with arterial ischemia (12,13), but in recent studies, it has been increased to up to 46% (8,10). Thrombotic events occur in 31% of COVID-19 positive patients. Mortality rate in ischemic patients is 5-9% (8,9) and in ischemic patients with COVID-19, it increased to 50% (10). This may reflect the fact that hypercoagulopathy in SARS-CoV-2 patients is a predictor of poor prognosis. The most common ischemia in patients with coronary artery disease was 71% of lower extremity ischemia, followed by 14% of upper extremity, 12% of multiple locations, 10% of cerebral ischemia and 14% of intestinal ischemia (10), respectively.

In 45% of patients, ischemia occurred first and then COVID-19 is diagnosed, and in 55% of cases, ischemic events occurred during hospitalization due to COVID-19 (10). Among patients who experienced ischemia after admission to the hospital, symptoms revealed between 1 to 5 or 5 to 10 days after hospitalization (average 6 days) (10). Confirmation of ischemic events among COVID-19 positive patients in the mentioned large study was 51% with computed tomography angiogram (CTA) and in 39% with Duplex ultrasound (10). The diagnosis of acute ischemia was made only with clinical signs in 10% of cases due to the instability of the patients (10).

In this study, patient's ischemic symptoms appeared 4-5 days after hospitalization, the diagnosis was first made by clinical symptoms. Doppler ultrasound was performed on the patient's bedside according to his condition. The patient then was taken to the operating room, due to the progression of thrombosis. CTA was performed to confirm the diagnosis and patient needed to transfer back to the operating room. Due to the progression of thrombosis, multiple organ failure symptoms and deterioration of the patient, Doppler ultrasound was performed again on his bedside, which confirmed the progression of thrombosis and its spread to the abdominal aorta and renal arteries. Although the patient had IABP, which can increase the risk of ischemic thrombosis, he was taking a high dose of heparin, aspirin and Plavix. Clot removal surgery, thrombosis formation and its rapid spread have not been associated with any thrombosis following IABP and indicates hypercoagulable state conditions.

Treatments for lower extremity ischemia in COVID-19 positive patients include revascularization (27%), primary amputation (10%), administration systemic tissue plasminogen activator (tPA) (6%) and systemic anticoagulation (57%). Eventually, 18% of them lost their limb and 46% of patients died in hospital (10). Perini et al (14) reported a patient with COVID-19 and acute limb ischemia who developed Acute iliac limb ischemia. Open thrombectomy was performed but re-thrombosis happened and the patient died soon after. In another study conducted by Bellosta et al (7) on 20 patients with COVID-19, different treatment methods such as;
popliteal angioplasty, femoral endarterectomy, kissing iliac stent, intraoperative thrombolysis were evaluated, which eventually led to re-thrombosis. Around 93% of patients had limb amputation and 40% of deaths were reported within 1-2 days. There is currently no standard treatment for limb thrombosis following COVID-19. Systemic tPA and catheter-directed thrombolysis have been suggested as rapid treatment options, but these methods are contraindicated in surgical patients. However, due to poor prognosis and lack of appropriate treatments, thrombolytic regimens have also been suggested as off-label use (15).

Conclusion
In general, there are still not many COVID-19 positive patients who need open heart surgeries, therefore our information about treatment of limb ischemia in this group is not sufficient and the mortality rate is high. Off-label treatments may need to be reconsidered. It is hoped that by reporting similar cases and gathering information, effective treatment can be found and more patients can be saved.

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Authors’ contribution
MBM was the head of the surgical team who managed this complication. ZAA and HG were the members of surgical team and participated in data collection. SAM was a major contributor in the literature search and preparing the discussion. HG participated in drafting of the manuscript, administrative, technical and material support. ZAA edited the final draft. All authors edited the final draft and final approval of the manuscript.

Conflicts of interest
The authors declare that they have no competing interests.

Ethical considerations
Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors. Informed consent was obtained from the patient for publication of this report.

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