Case Report

High thrombus burden despite thrombolytic therapy in ST-elevation myocardial infarction in a patient with COVID-19

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Consideration of thrombolysis as first-line reperfusion therapy in patients with COVID-19 and STEMI is recommended by ACC/SCAI guidelines. We describe a patient with COVID-19, who presented with ST-elevation myocardial infarction and was treated with thrombolysis and anticoagulation. He was later found to have a significant persistent thrombus burden requiring thrombectomy and stent placement. Invasive hemodynamics on multiple high-dose pressers revealed a high cardiac output state with low systemic vascular resistance, consistent with distributive rather than cardiogenic shock. Our case illustrates that thrombolytic therapy alone may not be adequate in patients with STEMI and COVID-19, as well as the importance of early invasive hemodynamics in management of shock in patient with STEMI and COVID-19 infection.

Keywords
COVID-19; acute coronary syndrome; ST-elevation myocardial infarction; thrombolysis

1. Case report

A 59-year-old man with a history of diabetes, hypertension, and hyperlipidemia presented to the emergency department with substernal chest pain. He also reported a two-week history of cough, pleuritic chest discomfort, and night sweats. On the night prior to admission, about 14-16 hours prior to arrival in the ED, he developed intermittent substernal chest pain, which spontaneously resolved. Chest pain recurred 90 minutes prior to presentation and remained constant and severe, prompting his family to call paramedics. On arrival, he was afebrile, normotensive, bradycardic to 46 beats per minute, tachypneic to 35 breaths per minute, and hypoxemic saturating 75% on 15 L of oxygen via non-rebreather. Patient was ill-appearing and emergently intubated for worsening respiratory distress and hypoxemia.

Initial EKG (Fig. 1A) showed complete heart block (CHB) with a junctional escape rhythm, ST elevations concerning for inferolateral ST elevation myocardial infarction (STEMI). Q waves were evident in the inferior leads, and initial troponin was elevated to 25 ng/mL, suggesting a delayed presentation. Other laboratory tests (Table 1) showed leukocytosis to 12,760 cells/L with a left shift and no lymphopenia, increased creatinine level of 1.90 mg/dL, and elevated inflammatory markers including ferritin (2,634 ng/dL), C-reactive protein (259 mg/L), D-dimer (3.52 ng/mL FEU), and interleukin-6 (26 pg/mL). Chest x-ray showed patchy bilateral infiltrates concerning for COVID-19 pneumonia. Chest CT angiography excluded pulmonary embolus and aortic dissection, confirmed bilateral infiltrates. Transthoracic echocardiography showed severely reduced left ventricular ejection fraction of 25% with marked inferolateral wall motion abnormality, mildly depressed right ventricular systolic function, no significant valvular dysfunction, and no pericardial effusion.

Patient received loading doses of aspirin and ticagrelor with heparin bolus and drip with a plan for emergent percutaneous coronary intervention (PCI). However, due to a concurrent hemodynamically unstable STEMI occupying the catheterization lab and an anticipated delay of greater than 120 minutes to invasive management, chemical thrombolysis was ultimately...
Figure 1. EKG progression throughout hospitalization. A) EKG on admission, B) EKG one hour post-thrombolysis, C) EKG 2 days post-PCI.
PCI: percutaneous coronary intervention.
selected as initial reperfusion strategy. Alteplase 15 mg was infused over one minute, followed by 50 mg over 30 minutes, and 35 mg over 60 minutes.

EKG after thrombolysis (Fig. 1B) showed interval improvement of ST elevations. Given the greater than 50% improvement in ST elevations in the inferior leads and resolution of ST elevations in the lateral leads, thrombolysis was considered successful.

The patient was hypotensive and transferred to the intensive care unit on dopamine, norepinephrine, and vasopressin. Given the EKG improvement after the administration of thrombolysis and significant bilateral consolidations on CT chest, shock was attributed toward most likely mixed cardiogenic and distributive shock from his underlying pulmonary infection. Troponin peaked at > 440 ng/mL. RT-PCR collected on admission returned positive for SARS-CoV-2.

Cardiac catheterization was performed 48 hours after thrombolysis due to persistent mixed shock. Coronary angiography revealed subacute appearing thrombosis in two coronary territories, left circumflex (LCX) and right coronary artery (RCA). A large thrombus was identified in the proximal-to-mid LCX, resulting in 90% obstruction with TIMI-3 flow (Fig. 2). A clear atherosclerotic lesion could not be identified. The RCA was an ectatic, large, dominant vessel with thrombic occlusion in the distal vessel just after the take-off of the posterior descending artery, which remained patent but was a small (1 mm) vessel with TIMI-2 flow (Fig. 3). There did not appear to be any collateral flow to the distal RCA territory. Mild non-obstructive coronary artery disease was seen in the left anterior descending artery and ramus intermedius. Extensive clot was extracted from the LCX by aspiration thrombectomy. However, due to incomplete removal and persistent occlusion, a single drug-eluting stent was placed with 0% residual stenosis and maintenance of TIMI-3 blood flow (Fig. 4). The RCA was not intervened upon as the territory was thought to be non-viable due to inferior Q waves noted on EKG.

Prior to PCI, on positive pressure ventilation (5 cmH$_2$O) and vasopressor support, right heart catheterization (RHC) identified the following intracardiac pressures: mean right atrial 9 mmHg, right ventricle 42/5 mmHg, pulmonary artery 42/18 (26) mmHg, and mean pulmonary artery capillary wedge 17 mmHg. Per thermodilution, the mean cardiac output was 8.2 L/minute and mean cardiac index was 3.97 L/min/m$^2$, with a systemic vascular resistance (SVR) of 721 dynes, suggesting a high cardiac output state and low SVR on background vasopressor support more consistent with a predominance of distributive versus cardiogenic shock as a primary mechanism for his hypotension.

The patient received empiric broad spectrum antibiotic coverage for possible secondary bacterial pneumonia. Due to fevers and worsening oxygen requirements on hospital day 3, he received one dose of tocilizumab 400 mg IV off-label for presumed COVID-19-induced cytokine storm. Given his severe thrombus burden, heparin was continued postcatheterization.

The patient's hemodynamics gradually improved, with atria-
Figure 3. Coronary angiogram of right coronary artery. LAO projection showing an ectatic proximal to mid right coronary artery with mild nonobstructive disease (Star) and a distal vessel with evidence of thrombus prior to the takeoff of the posterior descending artery (Arrow). LAO: left anterior oblique.

Oxygen requirements improved, and he was extubated on day 13. The patient was discharged on hospital day 19 on apixaban and ticagrelor and, on follow-up phone conversations, continues to improve symptomatically.

2. Discussion

Currently, pathophysiology of the COVID-19 virus is incompletely understood thus creating clinical management challenges. Hypercoagulability and increased rate of arterial thrombosis in multiple vascular beds, including coronary thrombosis causing STEMI, has been observed in patients with COVID-19 (Tan et al., 2020; Tang et al., 2020; Zhang et al., 2020). Proposed mechanisms of hypercoagulability and arterial thrombosis include development of antiphospholipid antibodies, complement-mediated endothelial injury, and plaque destabilization due to systemic inflammation (Campbell and Kahwash, 2020; Xiong et al., 2020; Zhang et al., 2020). Consideration of thrombolysis for first-line treatment of STEMI in order to decrease catheterization lab exposure has been suggested for COVID-19 positive patients in ACC/SCAI guidelines (Welt et al., 2020). A case series of STEMI in COVID-19 patients by Bangalore et al. (2020) observed inferior outcomes and a 100% prevalence of elevated D-dimer relative to STEMI patients with COVID-19 (Bangalore et al., 2020). Importantly, most of the patients in this series were managed with emergent cardiac catheterization and not thrombolysis, but notably still with poor outcomes. Bangalore et al. (2020) also found that 10 out of their 18 COVID-19-positive patients with ST elevations on EKG ultimately had noncoronary myocardial injury,
which is an important consideration to make when deciding whether to give thrombolytics to someone and exposing them to a higher risk of bleeding (Bangalore et al., 2020). It should be noted that, at the time of presentation, it was not known that the patient had a COVID-19 infection. At the time, due to the typical chest pain pattern and the EKG pattern, the pretest probability of coronary obstruction was high enough for this patient to proceed with thrombolysis. While our patient had risk factors for coronary artery disease, we believe that his presentation of heavy thrombus burden in two coronary distributions despite lytic therapy and anticoagulation may be out of proportion to his risk. We believe his coronary occlusions were due to simultaneous thrombotic occlusions triggered by the hypercoagulable state associated with COVID-19, indicating further evidence of a different pathophysiology causing STEMI in patients with COVID-19. Given the rapid practice changes related to thrombolytic therapy in the midst of the COVID-19 pandemic, we believe that this case demonstrates a need for increased caution in exclusively depending on thrombolysis in treating COVID-19 patients with STEMI, as our patient likely benefited from eventual percutaneous coronary intervention as well as continuation of anticoagulation therapy.

Additionally, RHC and invasive hemodynamics proved important in guiding management of this patient in his mixed shock state, as patients with concurrent COVID-19 infection and STEMI can have multiple etiologies for shock and respiratory failure. Despite this patient's large STEMI and severely reduced left ventricular systolic function, the invasive hemody-
Table 1. Initial laboratory values on admission

<table>
<thead>
<tr>
<th>Laboratory Values</th>
<th>Result</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>White-cell Count</td>
<td>12,760 cells/mL</td>
<td>4,000-11,000 cells/mL</td>
</tr>
<tr>
<td>- Neutrophils %</td>
<td>74%</td>
<td></td>
</tr>
<tr>
<td>- Bands %</td>
<td>8%</td>
<td></td>
</tr>
<tr>
<td>- Lymphocytes %</td>
<td>11%</td>
<td></td>
</tr>
<tr>
<td>Troponin</td>
<td>25.33 ng/mL</td>
<td>&lt; 0.04 ng/mL</td>
</tr>
<tr>
<td>Creatinine</td>
<td>1.90 mg/dL</td>
<td>0.72-1.25 mg/dL</td>
</tr>
<tr>
<td>AST</td>
<td>220 U/L</td>
<td>5-34 U/L</td>
</tr>
<tr>
<td>ALT</td>
<td>65 U/L</td>
<td>0-55 U/L</td>
</tr>
<tr>
<td>Lactate</td>
<td>4.5 mmol/L</td>
<td>0.5-2.2 mmol/L</td>
</tr>
<tr>
<td>Lactate Dehydrogenase</td>
<td>1,246 U/L</td>
<td>125-220 U/L</td>
</tr>
<tr>
<td>Ferritin</td>
<td>2,634 ng/mL</td>
<td>21-275 ng/mL</td>
</tr>
<tr>
<td>C-Reactive Protein</td>
<td>259.2 mg/L</td>
<td>&lt; 5 mg/L</td>
</tr>
<tr>
<td>D-Dimer</td>
<td>3.52 ng/mL FEU</td>
<td>0.50-0.60 ng/mL FEU</td>
</tr>
<tr>
<td>Procalcitonin</td>
<td>0.43 ng/mL</td>
<td>&lt; 0.08 ng/mL</td>
</tr>
</tbody>
</table>

Dynamic values obtained supported a predominance of distribu-
tive shock, and use of temporary mechanical circulatory sup-
port or intra-aortic balloon pump counterpulsation were un-
likely to be of benefit.

In conclusion, this case demonstrates a multi-territory
STEMI in a patient with COVID-19, with extreme clot burden
despite thrombolysis and greater than 48 hours of heparin ther-
apy. Thrombolytic therapy alone in COVID-19-positive pa-
tients with STEMI, as proposed by national guidelines, should
be used with caution. Additionally, in the setting of mixed
shock, hemodynamic and volume management guided by RHC
could be an important tool in caring for these patients.

Authors’ contributions
Gayatri Setia MD – Data curation, writing – original draft,
writing – review & editing
Jeffrey Tyler MD – Data curation, writing – review & edit-
ing, Supervision, Visualization
Alan Kwan MD – Writing – review & editing, Data cura-
tion, Visualization
Josh Faguet MD – Writing – review & editing
Shilpa Sharma MD – Writing – review & editing
Siddharth Singh MD – Writing – review & editing
Babak Azarbal MD – Writing – review & editing, Supervi-
sion, Conceptualization
Rose Tompkins MD – Writing – review & editing, Concept-
ualization
Dinora Chinchilla MD – Writing – review & editing

Sara Ghandehari MD – Writing – review & editing, Supervi-
sion, Conceptualization

Ethics approval and consent to participate
As this is a case report intended for medical and educational
purposes, it does not meet regulation criteria necessitating IRB
approval, and therefore no IRB approval was obtained. Con-
sent for publication was obtained by the patient and the pa-
tient’s family.

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Conflict of interest
The authors declare no conflicts of interests.

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be the new target in treating COVID-19–related systemic throm-


