Subacute dual stent thromboses in a COVID-19-positive patient

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Abstract
The hypercoagulable state of COVID-19 is resulting in an increasing number of unexpected venous and arterial thromboses in patients. We report a case of subacute dual coronary stent thrombosis in the setting of COVID-19 and we provide a brief review of current management recommendations.

Keywords: ST-elevation myocardial infarction, STEMI, COVID-19, subacute stent thrombosis

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Case report
A 71-year-old gentleman with hypertension presented with ischaemic chest pain. He reported non-remitting chest pain reaching maximal intensity two hours before presentation. It was noted that he had been diagnosed with COVID-19 11 days earlier and was convalescing at home.

An electrocardiogram (ECG) revealed a posterior ST-elevation myocardial infarction (STEMI) (Fig. 1). He was normotensive but had Killip-2 heart failure with bibasal crackles and SPO2 of 88% on room air. The patient was loaded with 300 mg aspirin, 600 mg clopidogrel, 80 mg atorvastatin and 40 mg intravenous furosemide.

Angiography revealed a culprit lesion at the bifurcation of the obtuse marginal and atrioventricular groove continuation of the
left circumflex (LCx) artery. The left anterior descending artery was unobstructed and the right coronary artery (RCA) showed critical proximal disease with three severe sequential distal lesions (Fig. 2). The patient was loaded with an additional 7 500 U heparin and the LCx lesion was treated with a 3.5 × 28-mm Synergy® everolimus-eluting stent.

Despite TIMI-3 flow in the LCx, the patient experienced ongoing chest pain and a decision was made to intervene on the RCA with an Orsiro® 2.75 × 40-mm sirolimus-eluting stent. Despite a good final result, the patient had ongoing chest discomfort. Re-injection of the left coronary artery confirmed the stent being widely patent but with mild haziness at the side branch ostium. A tirofiban bolus of 38 ml was administered, followed by a continuous infusion of 14 ml/h for 24 hours.

Forty-six hours later, the patient reported recurrence of chest pain and the ECG revealed an infero-posterior re-infarction, with subsequent development of cardiogenic shock requiring a dobutamine infusion. Emergency angiography revealed subacute stent thrombosis (ST) of both the LCx and RCA stents (Fig. 3). An additional 7 500 U intravenous heparin and tirofiban bolus was administered.

Attempts to restore flow in the LCx with multiple low-pressure balloon inflations and thrombus aspiration were unsuccessful. Intracoronary metalyse was injected through a microcatheter, with restoration of minimal flow. The RCA was wired and intracoronary metalyse was administered via a microcatheter, with restoration of flow. The stents appeared well expanded. The patient was loaded with ticagrelor and transferred to the intensive care unit, where he required continued dobutamine and adrenaline infusions.
Echocardiography revealed a non-dilated left ventricle with a mildly impaired systolic function (40–45%), with an akinetic infero-postero-lateral wall and mild reduction in right ventricular function but no other mechanical complications. Despite continued support, the patient developed worsening shock and pulmonary oedema, with subsequent demise on the same day.

Discussion

Since the first reported case of COVID-19 in December 2019, there has been in excess of 470 million cases and 6.1 million fatalities. A hypercoagulable state has emerged as a prominent feature and is associated with high mortality rates. A recent review of a nationwide registry across 42 STEMI care networks reported a significant increase in ST in individuals with STEMI and COVID-19 compared to non-infected individuals (3.3 vs 0.8%, \( p < 0.001 \)).

During infection, the interplay between coagulation/antifibrinolysis versus anticoagulation/fibrinolysis is tipped in favour of thrombosis. The inflammatory response induces a prothrombotic milieu with activation of neutrophils and platelets and the production of ultra-large von Willebrand factor (VWF) multimers. Furthermore, hypoxia-inducible transcription factors promote the expression of plasminogen activator inhibitor-1 (PAI-1) and tissue factor. Another avenue by which hypercoagulability is induced is through down-regulation of angiotensin-converting enzyme 2 (ACE2) receptors during COVID-19. This results in increased levels of angiotensin II and PAI-I levels, which inhibit fibrinolysis.

ST is an uncommon complication following percutaneous
coronary intervention (PCI), affecting less than 1% of implants at 30 days. The low incidence is in contrast to the extremely high 30-day mortality rates, approaching 45%, in those affected. COVID-19 has modified the usual presentation of many diseases and ST is increasingly being recognised as a feature. In all reported cases, standard PCI protocols had been adhered to, but it appears that the hypercoagulable state still places patients at higher risk. To our knowledge, this is the first reported case of two stents thrombosing simultaneously.

No published guidelines advise on the management of anticoagulant therapy in the setting of ST or COVID-19. A recent publication reviewed some aspects of antithrombotic therapy in acute coronary syndrome/COVID-19 but no specific reference to ST was made.

Our recommendation would be: PCI results should be optimised with the liberal use of intravascular imaging techniques to mitigate any modifiable factors that are considered risk factors for ST. Additionally, drugs that induce the CYP3A4 system should be avoided. High-potency P2Y12 inhibitors (preferably prasugrel) should be favoured over clopidogrel because of less-frequent genetically acquired resistance and lower risk for drug interaction. Additional technologies to monitor haemostatic abnormalities, including visco-elastic haemostasis assays, P2Y12 reactivity tests, heparin-induced thrombocytopenia (HIT) assays and anti-Xa level monitoring should be utilised as clinically indicated.

The acute management of ST is similar to its management in COVID-19-negative patients, including early angiography, continuation of high-potency antiplatelet therapy, and a case-by-case consideration for thrombus aspiration, intracoronary tissue plasminogen activator, and the use of GPIIb/IIIa as a bail-out strategy. Depending on local availability, left ventricular assist devices or left ventricular venting can be considered to provide haemodynamic support in the case of cardiogenic shock.

**Conclusion**

This case report highlights some of the limitations of real-world practice where access to intravascular imaging was limited due to COVID-19 hospital protocols and advanced haematological assays may not be readily available. The opportunity to collect specimens for HIT assays, P2Y12-resistance assays and antiphospholipid antibodies was missed due to the patient’s demise so shortly after the ST.

Although not confirmative by way of exhaustive exclusion, we propose that this report of dual ST decreases the probability of local lesion/stent factors responsible for ST and adds credence to the already described pro-thrombotic state in COVID-19 infection. It is important for cardiologists to be aware of the emerging association that may present, even in non-fulminant presentations of COVID-19 infection. Further studies are warranted to guide on the management of this devastating complication.

**References**