Stent Thrombosis and COVID-19

The outbreak of the COVID-19 pandemic has changed people's lives in countless ways worldwide. In the medical environment, the involvement of the respiratory tract is vital, but no less important than the involvement of the coagulation cascade, causing thrombotic events. (1) Endothelial dysfunction, atheromatous plaque destabilization, cytokine release with hyperinflammation, and hypoxia aggravation have been postulated as the origins of coagulation disorders and subsequent disseminated intravascular coagulation, although much of this complex mechanism is unknown. Cardiovascular complications of COVID-19 include myocardial injury (up to 30% of the cases) and venous thromboembolic events (up to 20%). However, arterial thrombotic events have been described more recently. In Spain, extensive thrombosis in multiple coronary territories, and an increase in stent thrombosis during the COVID-19 pandemic have been reported. (2) Our purpose was to report a dramatic increase in stent thrombosis cases during the pandemic.

The first case was a male patient with a history of diabetes, renal failure, and non-ST-segment elevation myocardial infarction in July 2020, requiring implantation of 2 drug-eluting stents in the anterior descending artery (ADA). The patient progressed to bilateral pneumonia and was transferred to the Intensive Care Unit. Nasopharyngeal swab was performed, with a positive result for COVID-19. Later, the patient presented class IV angina and ST-segment elevation in the anterior wall. Stent thrombosis was confirmed, and balloon angioplasty, thrombus aspiration, intracoronary tirofiban, and 2 drug-eluting stent implants were performed, with positive technical results and clinical outcomes.

The second case was a 67-year-old male patient with a history of diabetes and active smoking, who presented with stress angina, and ischemia detected by gamma camera. In August 2020, the patient underwent catheterization, and a subocclusive lesion was found in the ADA and in the right coronary artery. Angioplasty with a sirolimus-eluting stent in the ADA, and angioplasty with two sirolimus-eluting stents in the right coronary artery on the third day were performed with positive outcomes. Eleven days after discharge, the patient was readmitted for sudden-onset angina at rest. ST-segment elevation was detected in the anterior wall; the patient was swabbed as per institutional protocol, and was then admitted to the interventional cardiology unit. Proximal stent thrombosis of the ADA was diagnosed. Balloon angioplasty was performed and partial vessel opening was achieved. However, the patient developed complex ventricular arrhythmia and ventricular fibrillation, and died in the general ward. Twelve hours after his death, the swab result was positive for COVID-19.

The third case reported was a 62-year-old male patient with a history of diabetes, who was admitted for non-ST elevation acute coronary syndrome. Coronary angiography revealed a big and dominant circumflex artery with severe diffuse disease. Angioplasty with 4 drug-eluting stents was successfully performed. The patient was swabbed as per institutional protocol and the result was positive for COVID-19. Postoperative course was good, and the patient was discharged. Six days later, he presented an episode of severe angina at rest. He went to another hospital, where ST-segment elevation in the inferior wall was detected, and died before undergoing catheterization.

In the reports and case series before the COVID-19 pandemic, the rate of coronary stent thrombosis worldwide was around 1% and 2.5%. (3)

The three cases reported were treated in centers with a high number of cardiac patients, a hemodynamic team with a high rate of monthly angioplasties and experience in its practice, and a rate of stent thrombosis of 0.67% in June-July, 2019. Globally –and also in our setting–, acute myocardial infarctions and elective angioplasties decreased between 40% and 80%, without specifying the mechanisms that measured this reduction, probably attributed in part to an excessive number of heart attacks and deaths at home not reaching health centers due to the pandemic. (4) In this context, the 3 cases of stent thrombosis in the period of June-July 2020 in COVID-19 positive patients represent an increase from 0.67% (1/148) to the current 5.66% (3/56) of all angioplasties (odds ratio 8.32, 95% CI 0.84-81; p [Fisher] = 0.0638). Despite the limitation of the low number of subjects analyzed, the results are alarming. Moreover, of the 6 patients positive for COVID-19 undergoing angioplasty due to coronary events, 3 had stent thrombosis and 3 presented events on stable plaques or atherosclerotic le-

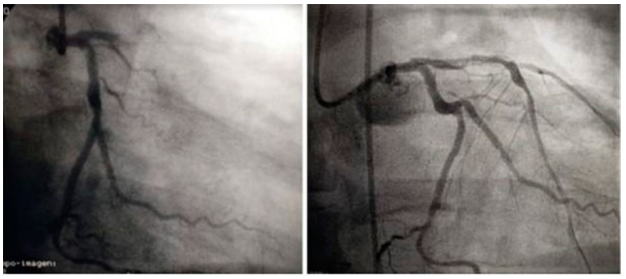

Fig. 1. Stent thrombosis in the anterior descending coronary artery on admission

Table 1. Characteristics of the three cases

	CASE 1	CASE 2	CASE 3
Age	55	67	62
Sex	Male	Male	Male
CRF:	HTN - DM	DM - Ex SMK - HTN	HTN - Ex SMK - DM - Overweight
Previous PTCA	July 2020 - ADA	August 2020 - ADA & RCA	July 2020 - CXA
Implanted stent	2 biodegradable polymer-based DES (Biolimus)	Sirolimus DES 3.5 × 33 2.5 × 23 – 3.5 × 18 mm	Everolimus DES x 4: 2.5 × 32 – 2.5 × 20 – 3.0 × 24 – 3.5 × 18 mm
Antiplatelet drug	ASA - Clopidogrel	ASA - Clopidogrel	ASA - Clopidogrel
Clinical COVID-19 codition	Bilateral pneumonia	Asymptomatic	Asymptomatic
COVID-19 diagnosis	PCR swab test +	PCR swab test + (sample taken on last admission)	PCR swab test + (sample taken as per protocol during hospitalization for PCI)
New coronary condition	Previous AMI	Previous AMI	Inferolateral AMI
CA	ADA Stent thrombosis	ADA Stent thrombosis	-
Time from previous PTCA	15 days	11 days	6 days
Treatment	Balloon thrombus aspiration Tirofiban 2 Sirolimus DES implanation	Balloon thrombus aspiration	-
Antiplatelet agent	ASA – Ticagrelor	-	-
Evolution	Good	Intraprocedural death	Death before admission to the catheterization laboratory

CRF: Cardiovascular risk factors. HTN: Hypertension. DM: Diabetes mellitus. SMK: Smoker. ASA: Aspirin ADA: Anterior descending artery. RCA: Right coronary artery. CXA: Circumflex artery. PTCA: Percutaneous transluminal coronary angioplasty. DES: Drug-eluting stent. AMI: Acute myocardial infarction. CA: Coronary angiography.

sions (personal data not previously published). Since no intracoronary ultrasound was performed to assess the stent thrombosis, the correct stent position and expansion cannot be confirmed, nor can previous hidden coronary dissections. Neither can it be confirmed that there has been intolerance to clopidogrel, polymorphisms associated with clopidogrel non-responders, or even that the three patients have omitted medication doses after hospital discharge. If our suspicion is confirmed, we should consider whether prasugrel or ticagrelor are more effective than clopidogrel for COVID-19-positive patients, whether we should increase the doses, whether all antiproliferative drugs in the stents interact in the same way with hypercoagulability associated with COVID-19, whether these phenomena observed in coronary stents are reproduced in stents implanted in other territories, (5) and many other questions for which not only do we have no answers, but we do not even imagine the questions.

Conflicts of interest

None declared.

(See authors' conflicts of interest forms on the website/ Supplementary material).

Ethical considerations

Not applicable.

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