

Case Report

Very Late Stent Thrombosis by Angiography. A Case of Atherosclerosis Progression by OCT

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ABSTRACT

The progressive nature of coronary atherosclerotic disease is often neglected in patients submitted to percutaneous coronary intervention. Very late (> 1 year) myocardial infarctions affecting the treated myocardial territory are usually attributed to device related complications. We report the case of a patient with acute inferior wall ST-elevation myocardial infarction, who had a thrombotic occlusion of a bare-metal stent implanted 8 years before. Despite the angiographic diagnosis of very late stent thrombosis, optical coherence tomography revealed that the acute myocardial infarction was caused by rupture of an atherosclerotic plaque outside of the previously stented segment.

DESCRIPTORS: Myocardial infarction. Percutaneous coronary intervention. Stents. Tomography, optical coherence. Coronary thrombosis.

The introduction of coronary stents, especially the drug-eluting, represented a great advance in the percutaneous treatment of coronary artery disease, making this intervention one of the therapeutic modalities most often performed in medicine.¹ However, in the mid-2000's, reports of a higher incidence of late thrombosis after implantation of first-generation drug-eluting stents gave rise to a series of debates on the long-term safety of these devices. In order to standardize the definitions and provide consensus recommendations for the classification of clinical outcomes after percutaneous coronary intervention (PCI), a document was published in 2007 by the Academic

RESUMO

Trombose Muito Tardia de Stent pela Angiografia. Um Caso de Progressão da Aterosclerose pela OCT

Em pacientes submetidos à intervenção coronária percutânea, a natureza progressiva da doença coronária aterosclerótica é frequentemente negligenciada. Geralmente, infartos muito tardios (> 1 ano) acometendo o território tratado são atribuídos a complicações relacionadas ao dispositivo. Apresentamos o caso de uma paciente com infarto agudo do miocárdio com supradesnivelamento do segmento ST na parede inferior, que apresentava oclusão trombótica de um stent não farmacológico implantado 8 anos antes. Apesar do diagnóstico angiográfico de trombose muito tardia, a tomografia de coerência óptica revelou que a etiologia foi a ruptura de placa aterosclerótica no leito distal, fora do segmento previamente tratado.

DESCRITORES: Infarto do miocárdio. Intervenção coronária percutânea. Stents. Tomografia de coerência óptica. Trombose coronária.

Research Consortium (ARC).² In brief, adverse events occurring in a previously treated area are attributed to the implanted device, until another clear cause is documented. In the specific case of stent thrombosis, the ARC provides the highest level of evidence for the diagnosis when there is angiographic documentation of thrombotic occlusion of a stent implanted in a vessel responsible for a territory under acute ischemia – the so-called definite stent thrombosis.

In this report, the authors present a case of a patient with acute myocardial infarction (AMI) with ST-segment elevation, in which the angiographic diagnosis of very

late definite thrombosis (> 1 year) of a bare-metal stent was ruled out by optical coherence tomography (OCT).

CASE REPORT

Female patient, 58 years old, had an AMI eight years before, when she was submitted to PCI with implantation of two bare-metal stents in the right coronary artery (RCA). Since then, she remained asymptomatic and her clinical evolution showed no new events. In June 2014, she was admitted to the emergency room of this hospital with typical chest pain, which had started at rest 2.5 hours before admission. Peripheral perfusion was adequate and there were no signs of pulmonary congestion. ECG showed ST-segment elevation in the inferior lateral and posterior walls (Figure 1).

The patient was treated with 300 mg acetylsalicylic acid, 600 mg of clopidogrel, and 5,000 units of unfractionated heparin administered intravenously, being promptly referred to the cardiac catheterization laboratory.

Coronary angiography was performed through the right radial access route, using a 6-F hydrophilic arterial sheath. The left coronary artery showed discreet parietal irregularities, with no obstructions (Figures 2A to 2C). The RCA was dominant, showed a stent in the proximal third that was patent, with diffuse hyperplasia and 40% luminal obstruction in its narrowest point, followed by occlusion with contrast retention inside another stent located in the distal third (Figure 2D), demonstrating definite and very late stent thrombosis.² The left ventricle showed moderate inferior hypokinesis (medio-basal) (Figures 2E and 2F).

After positioning the 0.014-inch guide wire on the RCA distal bed, the Export® thromboaspiration catheter (Medtronic Inc., Minneapolis, USA) was passed multiple times, covering the entire distal segment of the vessel, removing large amounts of thrombus and restoring Thrombolysis in Myocardial Infarction (TIMI 3) distal coronary blood flow. After administration of intracoronary nitroglycerin (200 µg), control angiography showed severe stenosis after the distal stent border, followed by

extensive ectasia of the vessel wall and filling failure images dispersed until the distal bifurcation, compatible with residual thrombotic burden (Figure 3A to 3C).

Due to the long segment affected in the distal stent portion, intracoronary OCT was performed to: (1) define the etiology of the vessel thrombosis (in-stent thrombosis or rupture of a distal plaque); (2) assess the extent of atherosclerotic disease in the distal segment of the vessel, impaired at the angiographic assessment due to the presence of residual thrombus; (3) identify adequate reference sites for stent positioning; (4) accurately measure the target-vessel size for better selection of devices to be implanted – the assessed segment showed large caliber disproportion between the ectatic and proximal and distal adjacent segments.

The OCT images were acquired using the commercially available Frequency Domain system (C7 XR®; St. Jude Medical, St. Paul, United States) during intracoronary injection of Hexabrix® ionic low-osmolarity contrast (Guerbet, Bloomington, United States) using a catheter guide with the help of a pump programmed to inject contrast at a constant speed of 3 mL/s for 3 seconds.

In the OCT images, adequate stent healing was observed, with complete coverage of the struts by tissue that had normal optical characteristics (Figure 3, panel 1). However, distal to the stent, a long segment with atherosclerotic involvement, of complex and heterogeneous composition, was observed. Eight millimeters after the stent distal border, it was observed the presence of fibrotic, focal plaque, promoting severe stenosis with minimal luminal area of 1.34 mm² (Figure 3, panel 2). At the entrance of the ectatic segment, the presence of a lipid-rich plaque was observed, with eccentric distribution and fibrous cap rupture (Figure 3, panel 3). The ectatic region had a mean diameter of 5 mm, almost normal morphology, and the presence of small eccentric fibrous plaque (Figure 3, panel 4). At the segments distal to the ectasia, the presence of a long lipid plaque that extended to the bifurcation was observed, with three additional sites of fibrous cap rupture (Figure 3, panels 5-7) and presence of

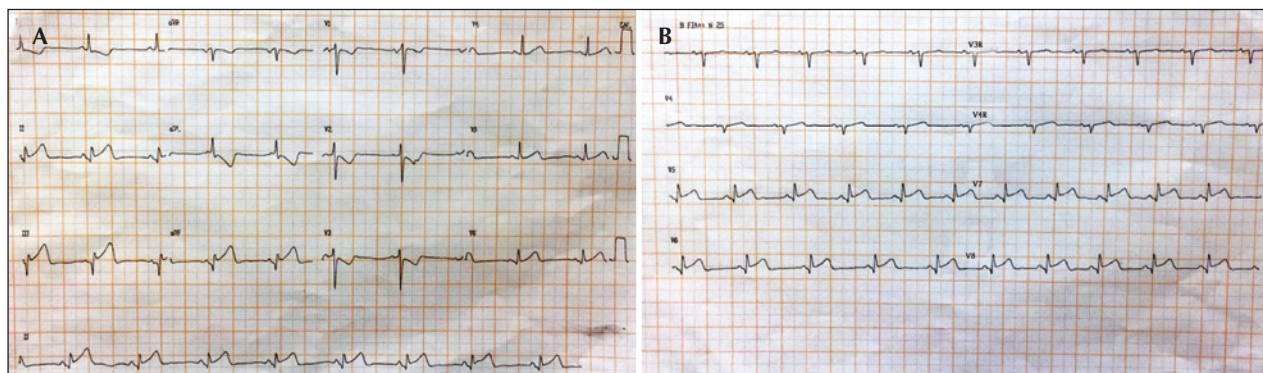


Figure 1 – Electrocardiogram at admission. ST-segment elevation is observed in the inferior, lateral, and posterior walls.

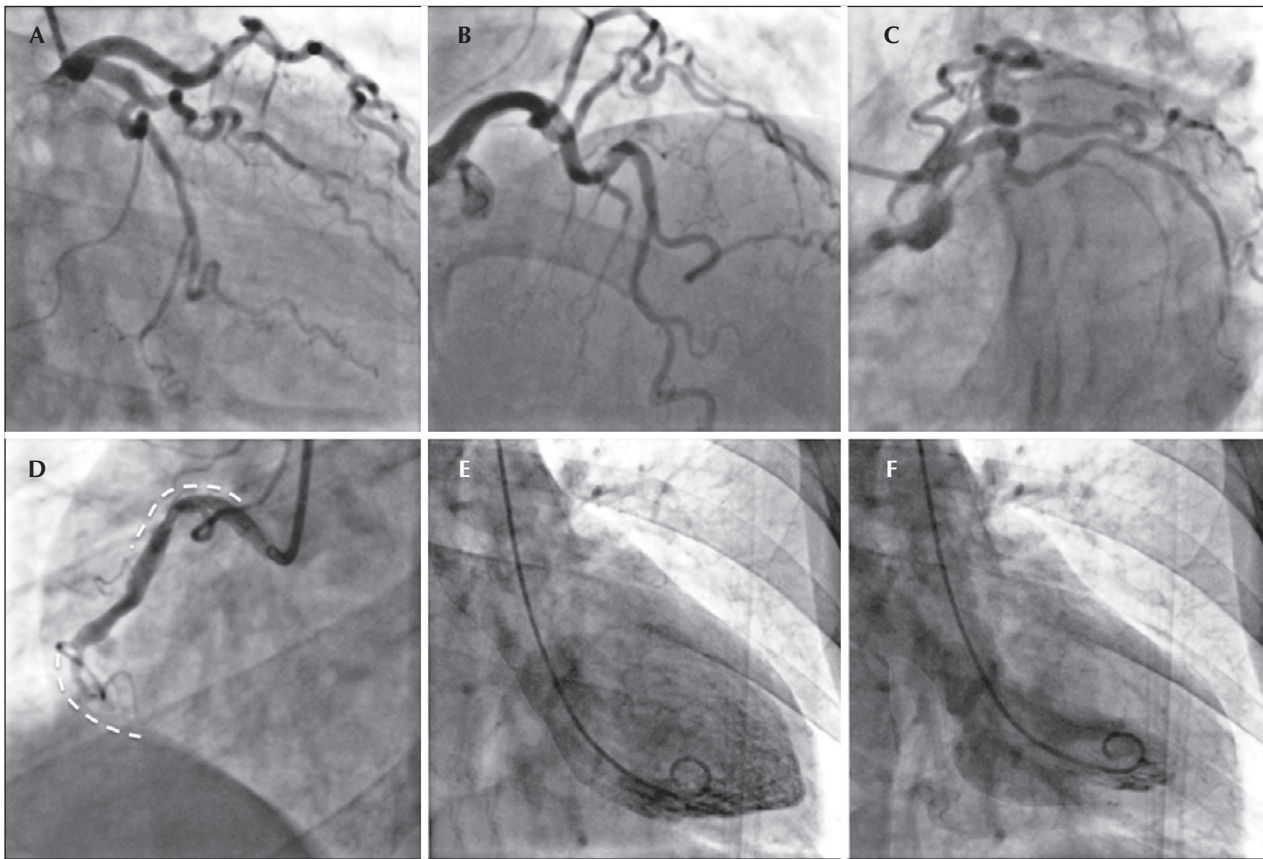


Figure 2 – Coronary angiography. Left main coronary artery with no significant obstructions (A, B, and C). Right coronary artery shows a thrombus inside the stent positioned in the distal third (D). Left ventriculography (E and F) show moderate basal and mid-inferior wall hypokinesis. Dotted lines indicate the sites of previously implanted stents.

residual thrombus in the carina (Figure 3, panel 8). The bifurcation showed an eccentric fibrotic plaque with luminal area of 2.21 mm² (Figure 3, panel 9), while the proximal third of the posterior descending branch was normal (Figure 3, panel 10).

After intravenous bolus administration of abciximab (0.25 mg/kg), the authors chose to treat the entire affected segment, covering from the bifurcation to the distal edge of the stent. Based on the measurements obtained by OCT, a 2.5 × 18 mm zotarolimus-eluting Endeavor Sprint® stent (Medtronic Inc., Minneapolis, United States) was implanted, positioned in the RCA towards the proximal third of the posterior descending branch, covering the bifurcation with the posterior ventricular branch (Figure 4A). This stent was post-dilated at its proximal portion using a 3.0 × 12 mm noncompliant balloon, inflated with high pressure (20 atm; Figure 4B), followed by post-dilation of the posterior ventricular branch with a 2.0 × 8 mm noncompliant balloon, inflated to 16 atm (Figure 4C). The implant optimization at the bifurcation was performed with simultaneous inflation of kissing-balloons (Figure 4D).

A second 4.0 × 30 mm Endeavor Sprint® stent was implanted proximally to obtain minimal overlap with the aforementioned stent and the previously existing stent (Figure 4E). Focal post-dilation with a 5.0 × 12 mm noncompliant balloon was performed only in the stent region positioned under the ectasia, aiming at adequate strut apposition (Figure 4F). Control angiography showed residual stenosis < 5%, hypertransparent image inside the treated segment, and TIMI 3 distal flow (Figure 5).

OCT assessment (Figure 5) showed adequate expansion and apposition of stent struts along the treated segment, including the ectatic region. However, the prolapse of a large amount of thrombotic material through the stent struts was observed in the region immediately proximal to the ectatic segment, affecting a short extension of 1.5 mm. Full coverage of the lesion was also confirmed, with minimal overlap of the recently implanted 4.0 × 30 mm stent struts on those of the previously existing stent, as well as adequate opening of the bifurcation at the posterior ventricular branch level, and absence of dissections in the posterior descending branch borders.

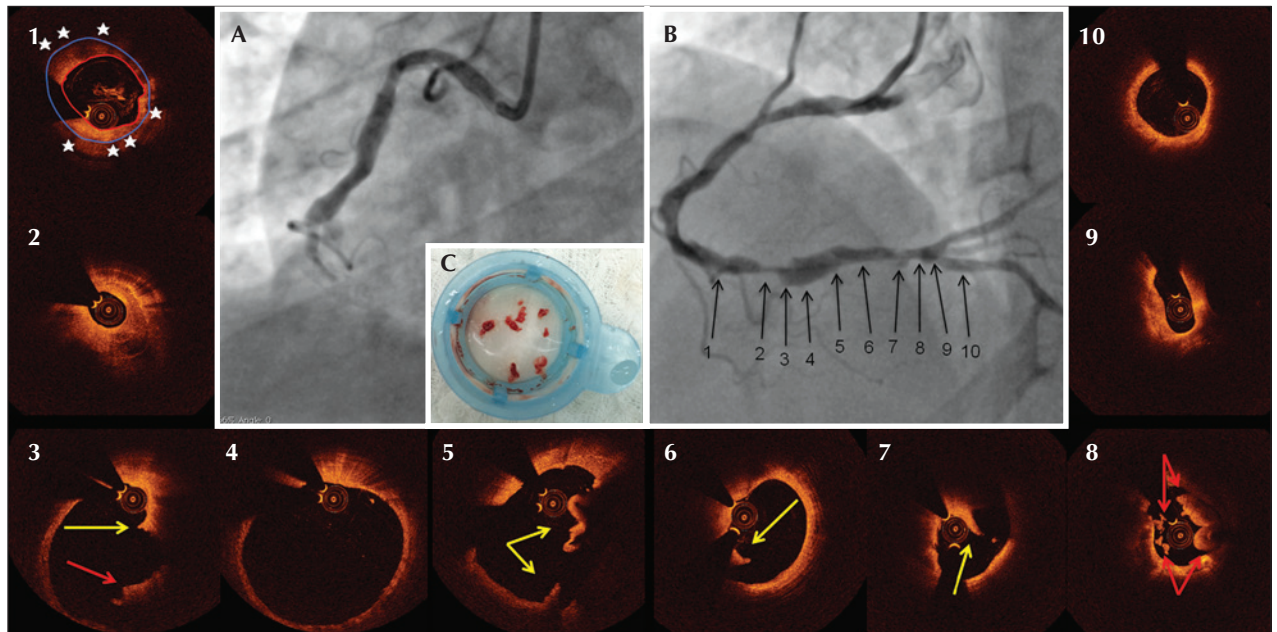


Figure 3 – Optical coherence tomography. The central panels show the right coronary artery before (A) and after (B) flow restoration. Thrombi removed during thromboaspiration (C). The stent in the distal third showed struts with homogeneous tissue coverage. The stent and lumen areas, indicated by red and blue contours, define the neointimal tissue with normal optical appearance (1). After the stent distal edge, stenotic fibrotic plaque can be observed (2). At the “shoulder” of the stenosis, a predominantly lipid plaque can be observed, with fibrous cap rupture and residual thrombus (3). The following ectatic segment is the vessel region with normal appearance (4). Distal to this segment, a lipid plaque, with multiple fibrous cap rupture sites, can be observed (5-7). At the bifurcation, there is large amount of thrombus (8), followed by eccentric fibrotic plaque (9). The proximal part of the posterior descending branch shows concentric intimal thickening (10).

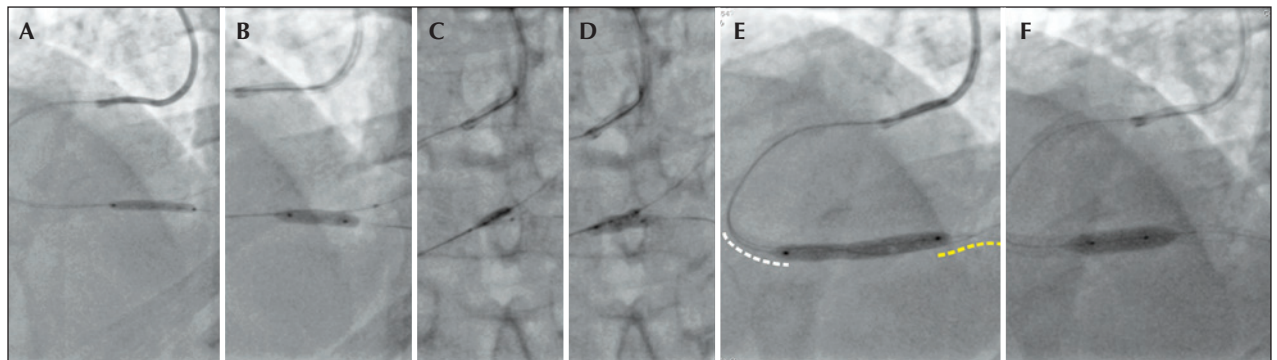


Figure 4 – Percutaneous coronary intervention. A 2.5 × 18 mm stent was implanted in the distal segment (A). This stent was post-dilated in its proximal part with a 3.0 × 12 mm noncompliant balloon (B). After the guide wires were repositioned, the posterior ventricular branch ostium was post-dilated with a 2.0 × 8 mm non-compliant balloon (C), followed by simultaneous balloon inflation in the posterior descending and posterior ventricular branches (D). Another 4.0 × 30 mm stent was implanted proximally, with minimal overlap with the previously implanted stent (yellow line) and the existing stent (white line) (E). Focal stent post-dilation, under the ectatic region, was performed with a 12 × 5.0 mm noncompliant balloon (F).

The electrocardiogram performed approximately 30 minutes after the PCI showed complete resolution of ST-segment elevation and absence of electrically inactive area. Glycoprotein IIb/IIIa inhibitor was maintained for 12 hours after the procedure. The echocardiography performed on the second day post-PCI showed an ejection fraction of 60% and mild hypokinesia of the lower and infero-lateral walls. The patient remained asymptomatic and was discharged on the 7^o day after AMI.

DISCUSSION

The association of AMI with angiographic documentation of thrombotic occlusion of a stent placed in a coronary artery responsible for the supply of a myocardial segment consistent with the topography of infarction constitutes a criterion for the so-called definite stent thrombosis, as well as having the highest specificity for the diagnosis of this phenomenon.² In the absence of angiographic documentation, an AMI that

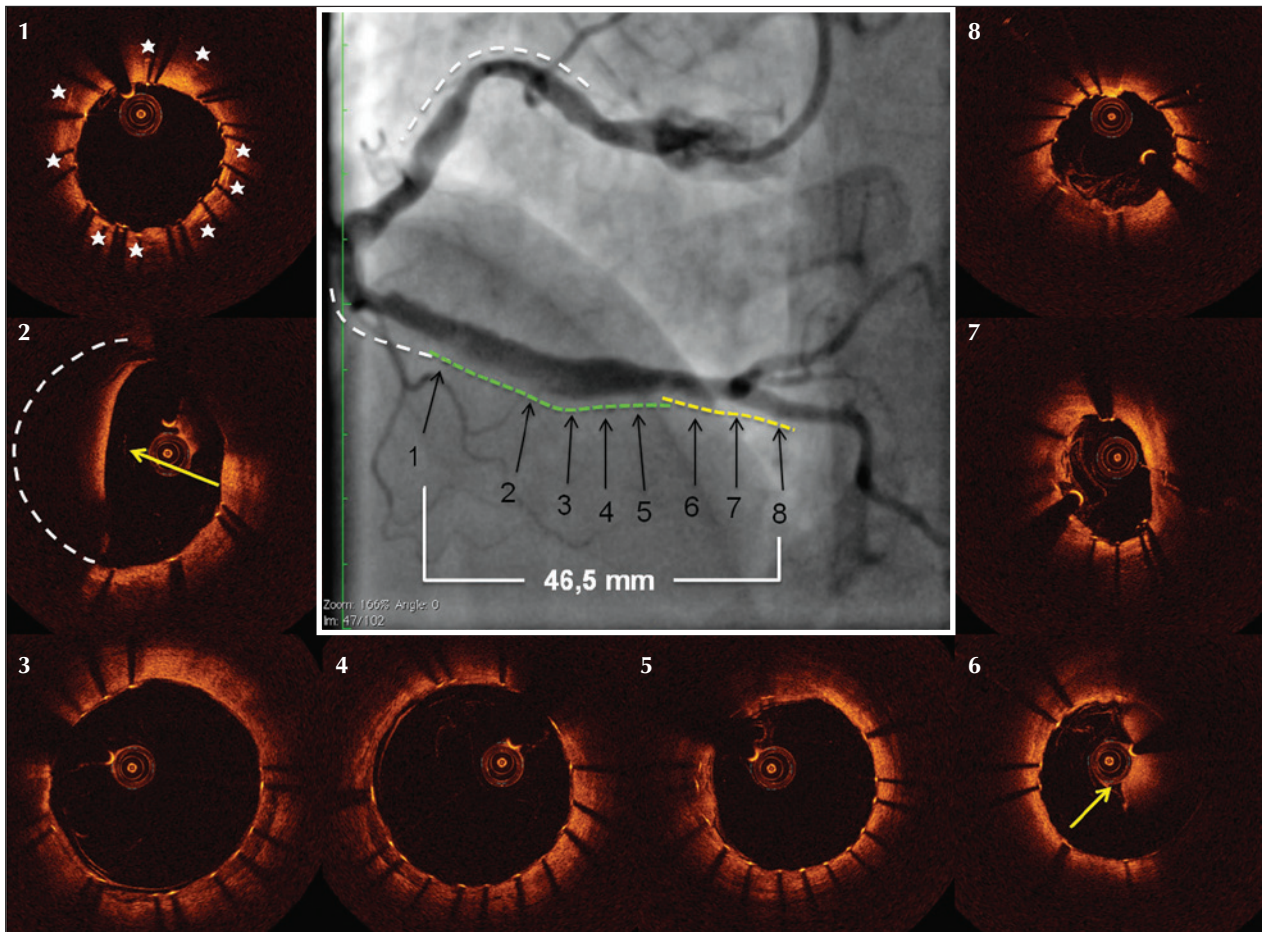


Figure 5 – Control angiography and optical coherence tomography. The previously implanted stents (white lines) and the newly implanted stents (yellow and green lines) show minimal overlap of the struts and complete segmental coverage. Panel 1 shows the location of the overlapping struts with the previous stent (asterisks). Thrombotic material prolapse can be observed, which explains the hypertransparent image on angiography (2). The focal post-dilation with a 5.0 × 12 mm balloon showed appropriate expansion and strut apposition in the ectatic segment (3 and 4). Outside the ectatic segment, the stent accompanies the size of the vessel (5). Next to the bifurcation, another point of thrombotic material prolapse is observed (6). Adequate stent expansion and apposition were attained at the bifurcation (7) and at its distal edge in the proximal third of the posterior descending branch (8).

is related to acute ischemia documentation in a previously treated territory, regardless of the time elapsed after PCI, establishes the diagnosis of probable stent thrombosis.² Although these criteria aim to increase the detection of adverse events related to previously implanted coronary stents, they cannot differentiate whether the event occurrence is really related to the device or if it is associated with the atherosclerotic disease progression outside the treated segment.

In this report, the authors present the case of a patient who developed AMI on the inferior wall eight years after being treated with the implantation of two bare-metal stents in the RCA. Although the coronary angiography showed arterial occlusion with a thrombus inside the previously implanted stent, the diagnosis of very late thrombosis was challenged by the findings obtained at the invasive assessment with OCT, which

showed that coronary thrombosis was due to the destabilization of a long segment of lipid-rich plaques located distally to the treated segment – and not to an accident related to the stent.

It should be kept in mind that coronary atherosclerosis is a diffuse, progressive disease and the treatment of a certain coronary stenosis does not change the natural history of atherosclerotic disease. Non-obstructive stenosis and/or those not causing ischemia in sites that are distant from the treated one at the time of the index procedure can progress in the future into high-grade stenosis with recurrent angina or destabilize, causing thrombosis and AMI.³ In an analysis of 1,228 patients treated with bare-metal stents, Cutlip et al.⁴ demonstrated that stent-related events predominated in the first year after implantation, becoming considerably rarer between the second and fifth years, when events related to the

natural history of atherosclerotic disease in other sites were highlighted. Recently, Leon et al.⁵ carried out a joint analysis of the TAXUS I, II,⁴ IV, and V studies, in which 1,400 patients treated with the paclitaxel-eluting Taxus Express[®] stent (Boston Scientific Corp., Natick, United States) were compared with 1,397 patients treated with bare-metal stents. While the annualized risk ratio for the occurrence of target-vessel revascularization in the first year was significantly lower in patients treated with the Taxus[™] stent (11.2% vs. 20.4%; $p < 0.0001$), target-vessel revascularization rates outside the previously treated segment were relatively constant, of approximately 2% a year between the second and fifth years of follow-up, and not significantly different between patients treated with Taxus[™] or bare-metal stents (3.3% vs. 3.8%; $p = 0.21$), more consistent with the natural disease progression than a specific stent-related effect.⁵

Although the coronary angiography is sufficient, in most cases, to differentiate in-stent restenosis from atherosclerosis progression outside the treated segment in stable patients, this case illustrates the difficulty of taining the angiographic diagnosis in the setting of acute coronary thrombosis. Even after obtaining the TIMI-3 flow with thromboaspiration, the angiographic luminogram did not allow the authors to establish the coronary thrombosis origin. The documentation of thrombotic occlusion inside the stent, together with a long segment of distal atherosclerotic disease, with areas of ectasia and stenosis, together with the considerable residual thrombus burden, constituted an additional confounding factor and highlighted the importance of diagnostic complementation with an invasive imaging method.

In this context, the OCT has a critical role that is superior to existing imaging methods. In addition to being the only imaging method capable of accurately assessing the degree of stent strut healing,^{6,7} OCT also allows for an accurate characterization of the atherosclerotic plaque components and their morphometric aspects. Particularly in the setting of acute coronary syndrome, OCT has high sensitivity (94%) and specificity (92%) for lipid plaque detection,⁸ and is the only *in vivo* imaging method capable of precisely quantifying the fibrous cap thickness⁹ and detecting the presence of inflammation with macrophage aggregates,¹⁰ morphological aspects that are crucial for characterization of the thin-cap fibroatheroma – identified as the “vulnerable plaque”, which most frequently leads to rupture and acute coronary occlusion.^{11,12} With the help of the OCT, it was verified that the stent was healed, with all its struts homogeneously covered by tissue with normal optical characteristics. Nonetheless, a long (~ 30 mm) segment of lipid-rich plaques with thin fibrous cap and multiple rupture points along its trajectory was identified, causing the formation of a large thrombotic burden, which accumulated upstream, occluding the coronary

flow inside the previously existing stent. Importantly, and in line with the previous literature,^{13,14} coronary thrombosis occurred due to rupture in plaques in lipidic non-stenotic segments, sparing the point of greatest narrowing, which showed the presence of a fibrotic plaque with preserved integrity.

Once the etiology was defined, the OCT was also very helpful to assess the disease extent and to identify reference regions for safe positioning of the stent borders. It is important to mention that the assurance of adequate and consolidated healing of the stent implanted eight years before allowed the team to treat only the distal vessel segment, without covering the previous stent with a new stent, a practice that possibly would not have been performed depending only on the angiographic assessment.

During primary PCI in AMI, stent implantation with low/moderate inflation pressures and less use of post-dilation are common practices, used to minimize the occurrence of the no-reflow phenomenon, which justifies, in part, the higher frequency of poor acute apposition in AMI, in comparison with PCI in stable patients.¹⁵ In this case, the OCT allowed the authors to know beforehand the actual dimensions of the vascular lumen throughout the entire segment, to understand the type of the underlying plaque, and evaluate the amount and location of residual thrombi. With this information, the authors were able to be more “aggressive” when selecting the diameters of the stents and balloons used during the procedure, aiming to maximize implanted stent expansion according to vascular dimensions and prevent any eventual strut malapposition. The use of a long stent with a 4.0 mm diameter and the performance of multiple post-dilations with balloons of different diameters at selected locations along the treated segment, including a 5.0 mm diameter balloon to optimize the central region of stent positioned under the vessel ectasia would certainly not have been the chosen strategies if the procedure had been guided by angiography alone. Nonetheless, this practice brings a higher risk of no-reflow. To minimize this risk, a glycoprotein IIb/IIIa inhibitor was added to the antithrombotic regimen, stent sizes were maximized in relation to vessel size, and focal post-dilations with short balloons were performed in the vessel segments that showed size discrepancy with the nominal size of the stent used, in addition to avoiding excessive manipulation in sites with higher residual thrombus burden. This strategy allowed the authors to obtain adequate stent expansion and strut apposition throughout the treated segment, at the expense of a short segment of thrombotic material prolapse through the stent struts, albeit without epicardial flow impairment. The success of this strategy was demonstrated by the complete regression of ST-segment elevation 30 minutes after the procedure and by the absence of akinesia in the affected wall on the echocardiogram, performed on the second day.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

FUNDING SOURCES

None declared.

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