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Case Report

Navigating Recurrent Acute In-Stent-thrombosis: Insights from a Single Admission Case Study

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Abstract:

However, only 48 hours later the patient started complaining of chest pain again. EKG showed new ischemic changes and a high sensitivity troponin of 5000. He was taken to the cath lab. LHC once again showed in-stent re-stenosis of the previously stented LAD and mid-ramus intermedius. He underwent balloon angioplasty to these stents. Post- LHC he was started on prasugrel and aspirin instead of the 2 previous left heart catheterizations when he was on clopidogrel and aspirin initially followed by ticagrelor and aspirin.

In addition to the dual antiplatelet therapy, he was also started on a Factor X inhibitor, rivaroxaban 2.5mg bid. Our hypercoagulability investigations did not yield any positive results, however, we found out the patient was on testosterone replacement.

This case is very unique in the fact that we had early re-stenosis of a drug-eluting stent and it did not only occur once, it occurred twice. One of the questions raised in this unique case is, when you have patients with early -restenosis of their stents, what is the preferred anti-platelet agent, and is a Factor Xa inhibitor indicated in this scenario? In the case of our patient, we went for prasugrel + aspirin + rivaroxaban and did not have any re-stenosis after that change to antiplatelet therapy.

Key words: duodenal adenocarcinoma, gastric outlet obstruction, gastrointestinal malignancy

Introduction

Case Presentation:

A 64-year-old Caucasian male was admitted to our hospital for a staged angioplasty and stenting procedure after a recent left heart catheterization which revealed a significant 80% stenosis of the proximal left anterior descending artery (LAD) and a significant 90% stenosis of the proximal ramus intermedius (Figure. 1)

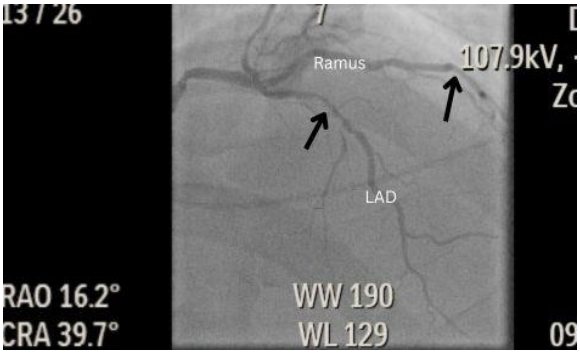


Figure 1: RAO cranial view showing significant stenosis (black arrow) to the proximal LAD and R1

The patient's pertinent past medical history included coronary artery disease status post recent right coronary artery (RCA) drug-eluting stent (DES) placement approximately two months prior, non-insulin-dependent type 2 diabetes mellitus, hypertension, hyperlipidemia, obstructive sleep apnea, generalized anxiety disorder, and hypogonadism on long term testosterone replacement therapy.

He successfully underwent a percutaneous transluminal coronary angioplasty (PTCA) with two DES placements in the mid-LAD and the mid ramus intermedius (Figure 2 and Figure 3) with post-procedure initiation of 90mg Ticagrelor and Aspirin along with guideline-directed medical therapy.

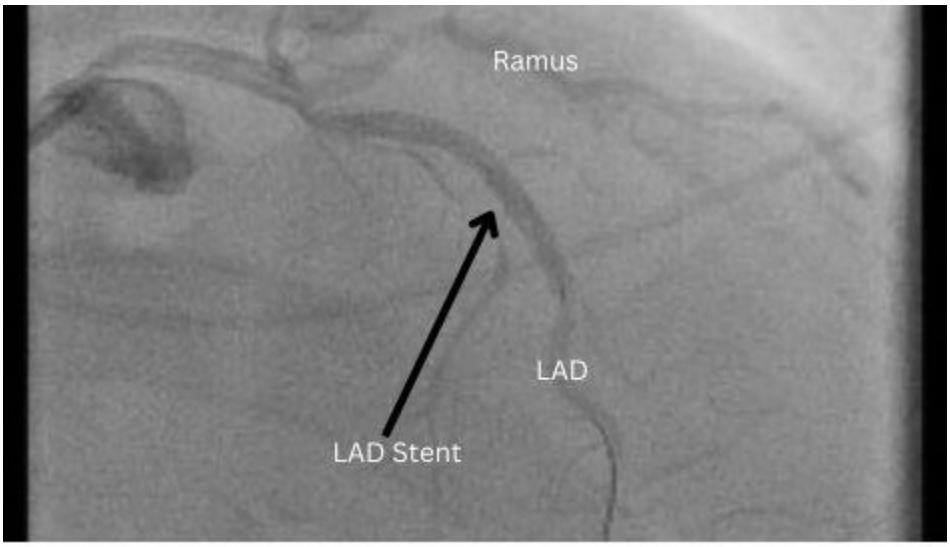


Figure 2: Angiographic image of the stented LAD

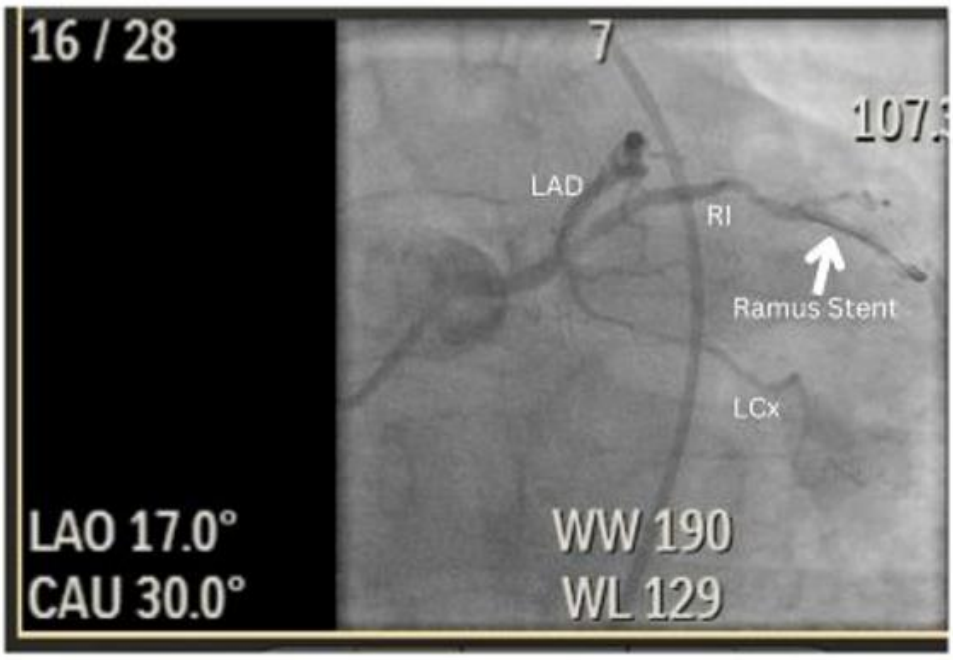


Figure 3: Left anterior oblique caudal view. This angiographic image shows the stented mid- ramus intermedius (white arrow).

Approximately six hours following the procedure, a rapid response was initiated for evaluation of patient reported chest pain. He described the pain as substernal pressure radiating up his left jaw and down his left arm. An initial EKG (Figure 4) was obtained which showed a normal sinus rhythm with ST elevations noted in leads II and AVF, both of which were identified on prior EKGs. Despite the administration of morphine, and multiple oral Nitroglycerin tablets followed by a nitroglycerin infusion, the patient continued to complain of worsening chest pain and became increasingly diaphoretic. A repeat EKG (Figure 5) was obtained which now demonstrated ST elevations in Leads I, aVL and V2-V6 with reciprocal ST-depressions in the inferior leads indicative of an antero-lateral ST-segment elevation myocardial infarction (STEMI).

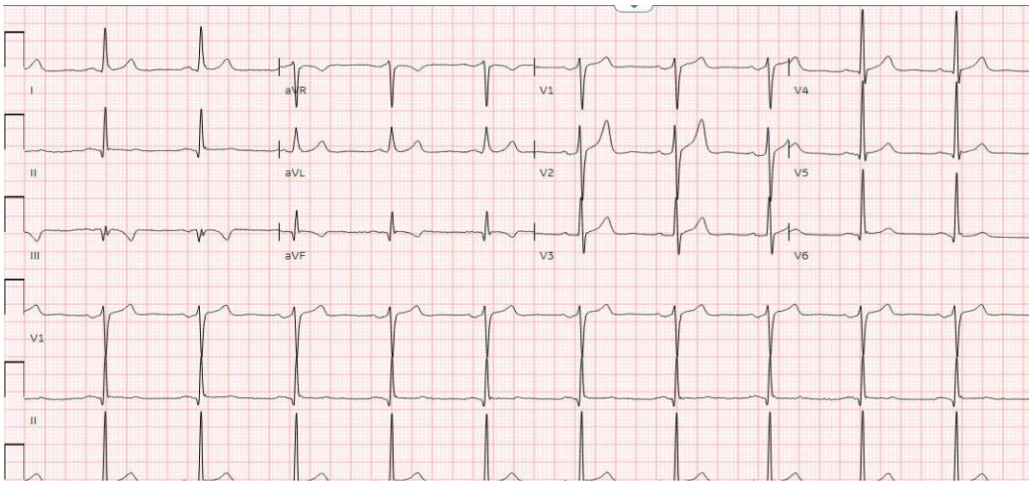


Figure 4: Initial ECG showing non-specific t-wave abnormalities seen in the inferior leads- Lead III and AVF

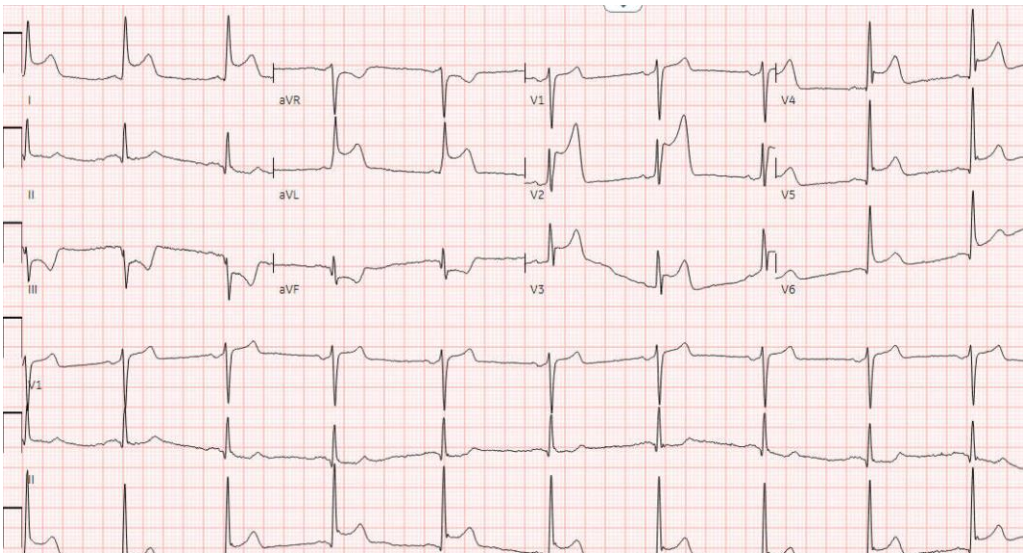


Figure 5: Repeat EKG showing ST elevations in Leads I, aVL and V2-V6 with reciprocal ST- depressions in the inferior leads

The catheterization lab was immediately activated, revealing total occlusion of the previously placed LAD and Ramus stents. (Figure 6)-A balloon angioplasty (Figure 7) was performed for both stents and the patient was transferred to the Cardiac critical care unit. In light of residual thrombotic burden and observed distal microvascular emboli during the PCI, the patient was initiated on an 18-hour duration eptifibatide (Integrilin) infusion along with the continuation of DAPT, comprising of aspirin and Ticagrelor, and GDMT (BB, High-intensity statin). A transthoracic two-dimensional echocardiographic assessment was conducted which revealed an EF of 20%, notably reduced from the 40% documented a month prior. This drop was presumed to be to a stunned myocardium; therefore, another transthoracic echocardiogram was ordered. Metoprolol and Entresto resumed.

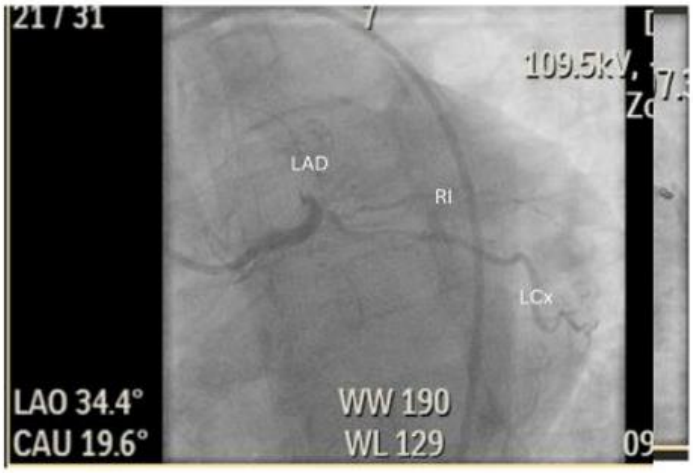


Figure 6: Left Anterior Oblique Caudal View showing a stenosed LAD and RI

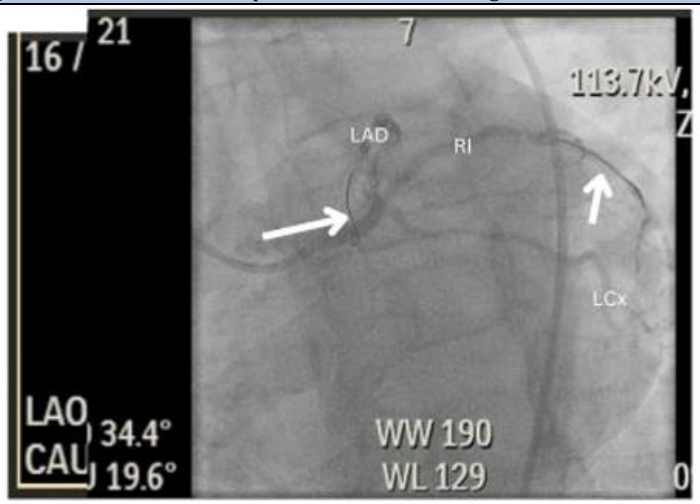
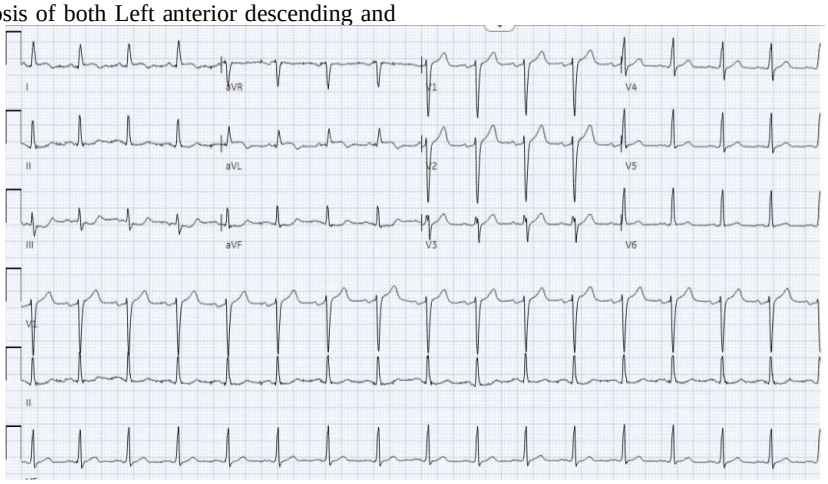


Figure 7: Left Anterior Caudal View Angiogram showing guidewire (white arrow) through the stenosed LAD and Ramus Intermedius.

Two days subsequent to his second percutaneous coronary intervention (PCI), another rapid response was called for the patient for complaints of classical anginal chest pain. An EKG was promptly obtained which showed mild STE in AVL with ST depressions in the inferior leads/III and AVF and a Hs trop of >5000. Given these findings, he was emergently transported to the catheterization laboratory and was found to have a recurrent late*** stent thrombosis of both Left anterior descending and Ramus Intermedius stents requiring PTCA and IVUS guided optimization of both stents (Figure 8). He was then placed on the eptifibatide infusion, and this time round was started on Prasugrel, instead of Ticagrelor, along with ASA. In addition, triple anticoagulation therapy was recommended for the patient and had 2.5mg rivaroxaban daily added to his Dual-Antiplatelet therapy.



At this point, the underlying cause for his recurrent late thrombosis was indeterminate however potential contributory factors such as stent under sizing, an underlying hypercoagulability disorder or sticky platelet syndrome were postulated. Consequently, a hematology consultation was sought to investigate the possibility of an underlying hypercoagulable state. A comprehensive hypercoagulable evaluation encompassing B12 levels, Folic acid levels, Homocysteine levels, Dilute Russell's Viper venom time (DRVVT), hexagonal phase phospholipid, protein C & S activity levels, Beta 2 glycoprotein, and anticardiolipin antibodies was performed. The results were significant for an elevated HCY level with a normal folate and high B12. The remaining of his workup resulted back negative.

Subsequent therapeutic interventions included the initiation of Vitamin B12 at a dosage of 500 mcg daily, vitamin B6 at 50mg daily, and folic acid at 1g daily. Furthermore, the hematology team recommended discontinuation of the patient's testosterone replacement therapy, given potential concerns regarding its relation to possible anti-platelet resistance. Additionally, the case was discussed with a representative from the drug-eluting stent (DES) manufacturer, Synergy, who reported rare instances of allergic reactions to the stent's coating and therefore recommended the addition of Benadryl to his medication regimen.

Discussion:

Despite the technological advances made concerning drug-eluting stents, there is still a need for revascularization of these stents at 1%- 2% per year. PCI for ISR currently constitutes about 10% of all PCIs done in the USA [1].

DES-ISR(in-stent restenosis) complications can be early (< 1-year post-procedure) or late (>1 post-intervention) [2]. Lei et al, conducted a retrospective study in 171 patients using optical coherence tomography (OCT) to evaluate characteristics of early vs late ISR in 2nd generational DES, reporting minimum stent area (MSA)<4.0 mm2 with a heterogeneous composition of the non-atherosclerosis present in early ISR [3]. Mechanisms underlying ISR could be linked to the stented vessel affected by the following factors: stent-related (undersized stents, or stent fractures), extra-stent (inhibited stent expansion due to calcification or multiple stent layers), and intra-stent factors (such as excessive tissue growth) [1]. While neointimal hyperplasia is found in bare metal stents (BMS), neo-atherosclerosis is a distinguished feature of DES, however, studies using OCI found that neo-atherosclerosis occurs in late DES-ISR (> 1-year post-intervention) [4-6]

Although the implementation of DES devices might have reduced the emergence of stent thrombosis (ST), it still exists [7]. These patients present with acute coronary syndrome, a history of diabetes, impaired left ventricular systolic dysfunction, impaired platelet reactivity, and lesions involving high anatomical complexity leading to increased chances of ST [8, 9]. As per the analysis conducted by PESTO, PRESTIGE, and Bern registries, in acute ST (<1 month), 50% of cases were due to uncovered struts, 35% cases were due to malapposition,10% were due to underexpansion and 5% due to edge diseases [10-12]. In addition, endothelial inflammation leading to hypercoagulable conditions and an overactive platelet cascade could also be a trigger for ST [13, 14]. A prospective study was conducted in Korea assessing the safety and efficiency of SYNERGY stents in 703 patients, yielded ST to be 3(0.4%) with 2 patients presented acutely and one in the sub-acute time frame [15]. Although the demographics of our patient differ from this study, genetics could be a risk factor for ST. Shoji et al, conducted a case-controlled study to evaluate the association of genetic loci and the occurrence of EST (early stent thrombosis <1 month), LST (late stent thrombosis > 1 month but <1 year), and VLST (very late stent thormbosis>1 year) identifying single nucleotide polymorphisms (SNPs) such as NSD1 (rs565401593 and rs561634568) were related to EST, while SNPs in GRIN2A (rs532623294 and rs199546342) were related to LST/VLST [16]. This study states that polygenic risk scores(PRS) were moderately predictive of EST and can serve towards risk stratification of ST [16].

Post-PCI complications of ST are managed by aspiration thrombectomy and angioplasty during angiography [13]. The patient must be switched to a potent anti-platelet therapy like ticagrelor or prasugrel, imaging of the stent should be assessed by IVUS and OCT for stent conformity and medical compliance must be evaluated [13, 17-19].

Our patient experienced two episodes of ST in acute (<24 hours) and sub-acute (<48 hours) pattern with ischemic ECG Changes and positive cardiac biomarkers, medically managed by factor X inhibitor (Rivoraxaban), ASA, and Prasugrel following PCI. We want to emphasize, factor x-inhibitors as a suitable choice of anti-platelet therapy in special instances. These inhibitors are known to interrupt the intrinsic and extrinsic coagulation pathway, preventing thrombin generation, which is a key activator of primary(platelet-mediated) and secondary (clotting-mediated), thus, mitigating thrombus formation [20]. This is significant for patients with ACS, where elevated thrombus levels persist for 6 months after the 1st insult [20]. Studies have shown promising results in favor of using 2.5 mg of Rivaroxaban twice a day in addition to dual-antiplatelet therapy showed a significant reduction in stent thrombosis and mortality [21]. Another study highlights the importance of platelet reactivity and ST in 11714 patients with DES, out of which 51 developed EST [22]. Higher platelet reactivity was measured as P2Y12 reaction units (PRU) and aspirin reaction units (ARU)and was found to be independent predictors of EST within 30 days. So, a need to monitor platelet function is warranted in such patients [22].

Conclusion:

As the rates of left heart catheterization and percutaneous angioplasty rise, in-stent restenosis is a serious complication of these procedures and it carries a high rate of morbidity and mortality. Early recognition of ISR will help curb the morbidity and mortality associated with it. Testosterone replacement therapy might play in role in the causation of early ISR. There are other factors related to the lesion and patient history that predispose a patient to in-stent restenosis.

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