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CASE REPORT
Coronary intervention

Subacute saphenous vein graft stent thrombosis due to unusual drug interaction: a case report

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Background Stent thrombosis is a potentially lethal complication of coronary angioplasty and responsible for 20% of all post-angioplasty myocardial infarctions. Unusual causes may be overlooked and difficult to identify.

Case summary A 70-year-old male with history of triple aortocoronary bypass presented with acute inferolateral ST-segment elevation myocardial infarction (STEMI). Critical stenosis of the vein graft to the right coronary artery was revealed, and with the use of distal embolic protection device, successful angioplasty with stent was performed under double antiplatelet treatment with aspirin and ticagrelor. Two weeks later, he presented again at the emergency department with an acute inferolateral STEMI. Subacute stent thrombosis with complete occlusion of the stented vein graft was evident. Repeated balloon dilatations restored the flow stabilizing the patient; optical coherence tomography showed good stent expansion and apposition. Scrutinizing the patient's history, we discovered co-medication with carbamazepine that is a CYP3A4 inducer and reduces ticagrelor's effect. Switching to prasugrel ensured potent antiplatelet treatment, and the patient was discharged 5 days later. The 6-month follow-up was uneventful and free of symptoms.

Discussion Stent thrombosis has dire consequences, and the precipitating factors should always be investigated. Inadequate platelet inhibition secondary to non-compliance to therapy or resistance and suboptimal stent expansion/apposition are its main causes. Drug interactions are an underrecognized factor that may significantly alter the potency of antiplatelet drugs and also lead to stent thrombosis; thus, treatment is essential to be tailored to each patient comedication.

Keywords Acute coronary syndrome • Antithrombotic treatment • Case report • Stent thrombosis • Saphenous vein graft angioplasty

ESC curriculum 2.1 Imaging modalities • 3.1 Coronary artery disease • 3.2 Acute coronary syndrome • 3.4 Coronary angiography • 8.6 Secondary prevention

Learning points

- Saphenous vein graft angioplasty carries increased risk of thrombotic complications, and individualized preventive measure implementation is essential.
- Recognition of the mechanism of stent thrombosis should always be pursued to avoid future events.
- Drug interactions are not unusual, and tailored treatment based on comedications ensures adequate efficiency.

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Introduction

Stent thrombosis (ST) is responsible for 20% of all myocardial infarctions after percutaneous coronary interventions (PCI) and is defined as subacute if it occurs between 1 and 30 days after PCI.[1,2] Identifying the cause of ST is of outmost importance to prevent future events and ensure stent permeability. Intravascular imaging, especially with optical coherence tomography (OCT), is able to detect intraluminal thrombi and discriminate stent-related causes of thrombosis as well as guide interventional management.[3]

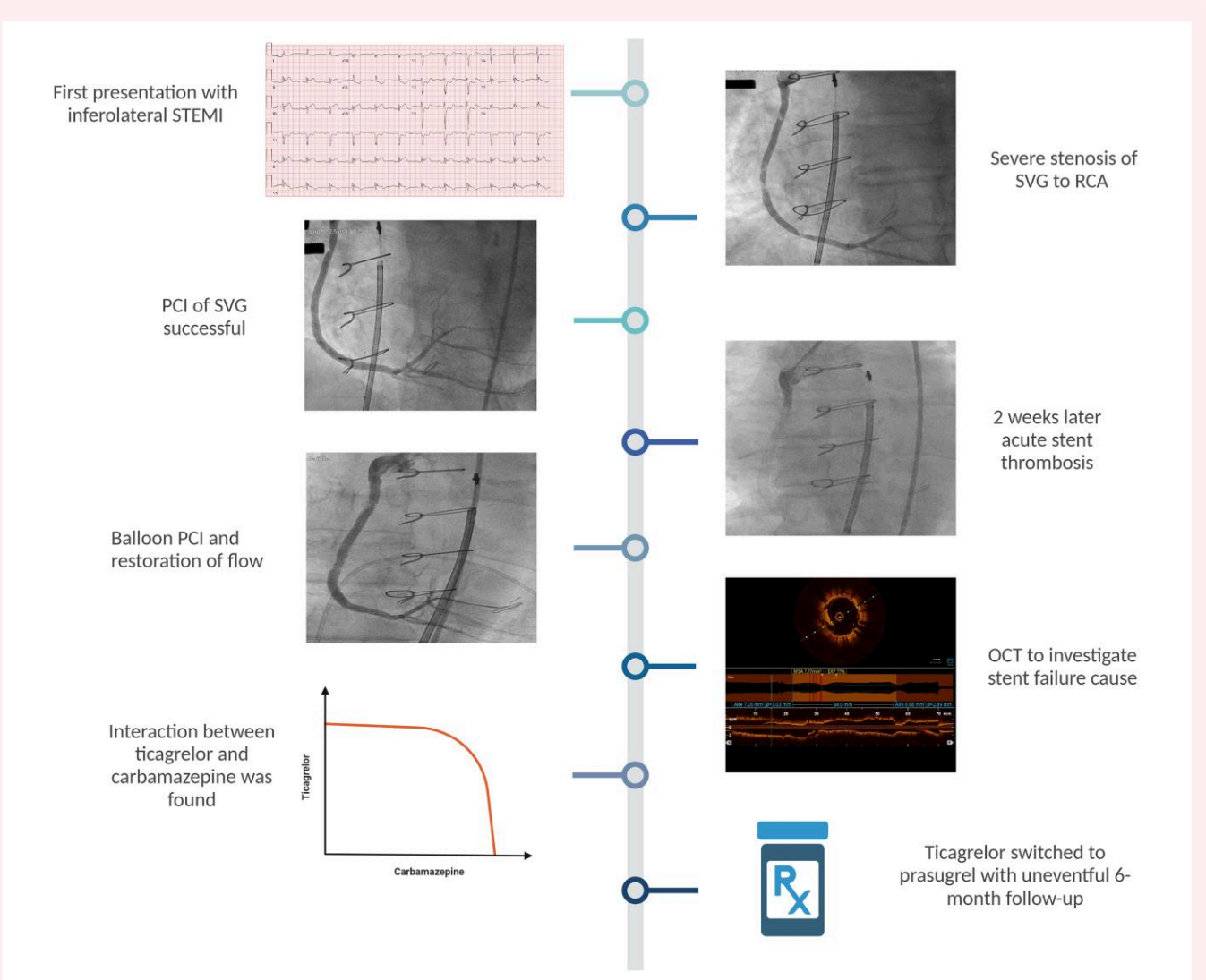
In this case report, we describe a case of subacute saphenous vein drug-eluting stent (DES) thrombosis, presenting as acute coronary syndrome leading to shock that was successfully managed. However, the cause was not evident until scrutinization of patient's medication history.

Summary figure

Graphical illustration of the event timeline. SVG, saphenous vein graft; STEMI, ST-segment elevation myocardial infarction; RCA, right coronary artery; OCT, optical coherence tomography.

Case presentation

A 70-year-old Caucasian male presented in the emergency department in late April with acute 2-h-onset chest pain. He was haemodynamically stable with apparent diaphoresis, and the electrocardiogram showed ST-segment elevation in the inferior and lateral leads (*Figure 1*). Cardiovascular examination was unremarkable. Being already under aspirin, he was loaded with 180 mg of ticagrelor and transferred immediately to the catheterization lab. His past medical history included triple aortocoronary bypass graft surgery 6 years ago for stable three-vessel coronary artery disease and implantable cardioverter defibrillator 2 years ago for primary prevention. The coronary angiography revealed patent left internal mammary artery to the left anterior descending artery that was occluded proximally, patent SVG to the severely stenosed first obtuse marginal branch, and sequential subtotal occlusions of the SVG to the occluded RCA (*Figure 2A*). Due to significant thrombotic burden, primary PCI of the SVG with distal embolic protection device (FilterWire©, *Figure 2B*) was performed. Direct stenting of the culprit lesion was successful with two overlapping stents (DES 4 × 28 mm and DES 4 × 16 mm). Considerable amount of thrombi was retrieved upon filter basket removal (*Figure 2C*). Final angiographic image revealed



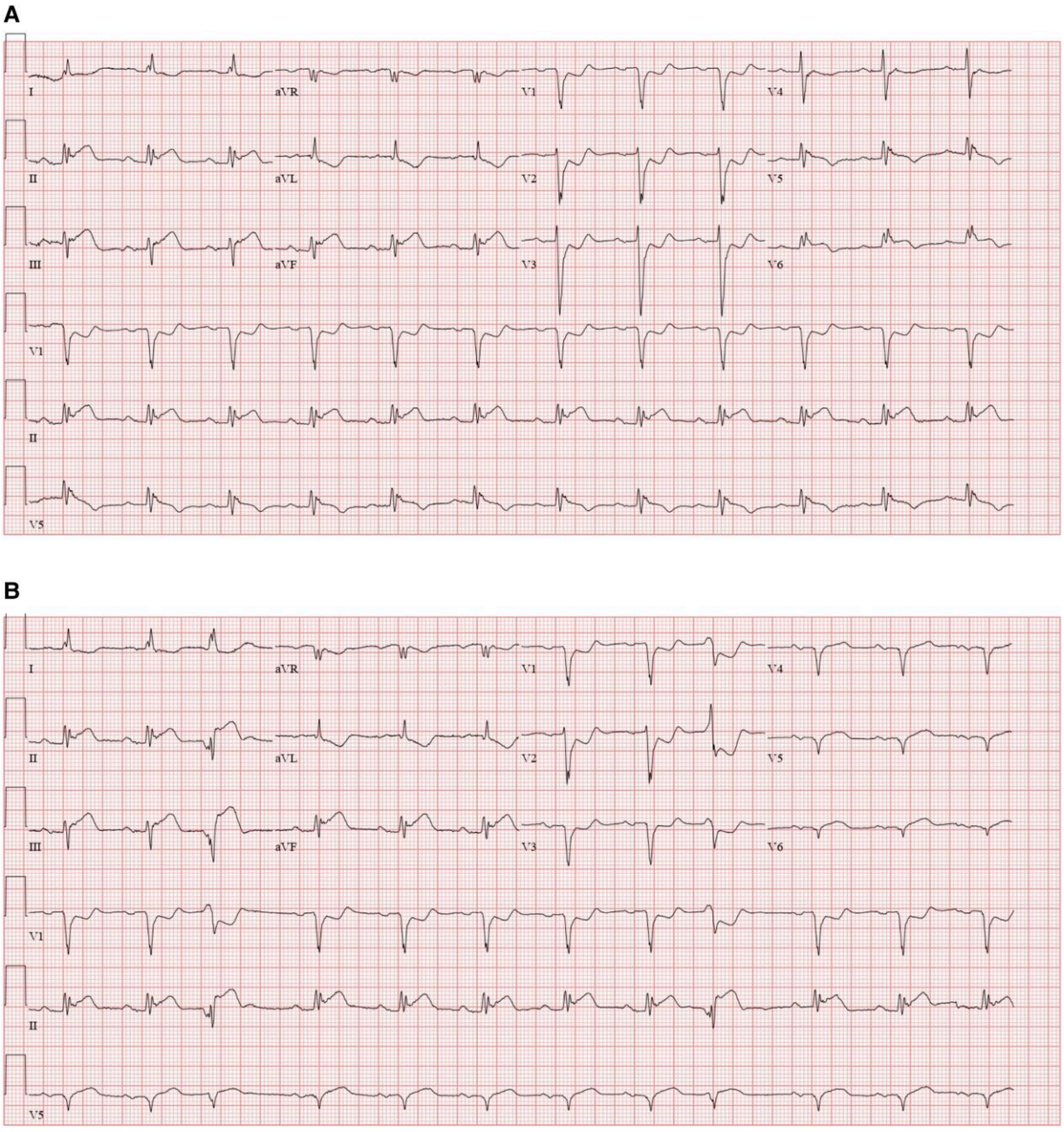


Figure 1 (*A*) Electrocardiogram at first presentation at the emergency department showing sinus rhythm and ST-segment elevation in leads II, III, aVF, V5, and V6 with reciprocal ST-segment depression in I, aVL, V1, V2, and V3 leads. (*B*) Electrocardiogram at second presentation at the emergency department with subacute stent thrombosis showing sinus rhythm with supraventricular extrasystoles, ST-segment elevation in leads II, III, aVF, V5, and V6 with reciprocal ST-segment depression in I, aVL, V1, V2, and V3 leads.

Thrombolysis In Myocardial Infarction (TIMI) flow 3 and no residual stenosis (*Figure 2D*). He was discharged 4 days later under double antiplatelet treatment with aspirin 100 mg o.d. and ticagrelor 180 mg b.i.d. His left ventricular ejection fraction was 45% with moderate inferolateral hypokinesia.

Two weeks later, he was urgently transferred to the hospital with acute-onset angina and ST-segment elevation in the inferior and lateral leads. Coronary angiography demonstrated complete occlusion of the stented SVG secondary to subacute ST (*Figure 3*). Unfractionated heparin along with IIb/IIIa glycoprotein inhibitor (eptifibatide) bolus dose was administered. Noradrenaline was administrated periprocedurally due to haemodynamic collapse. Balloon dilatations with a non-compliant 4.0 × 15 mm balloon were performed at the occlusion site and restored the flow to the vessel (*Figure 3*). Optical coherence tomography imaging after dilatations showed well-apposed and expanded stent with thrombotic remnants in the vessel (see Supplementary material online, *Video S1*). As the patient was free of symptoms and haemodynamically improved with tapered dose of noradrenaline, he was transferred to the acute cardiac care unit.

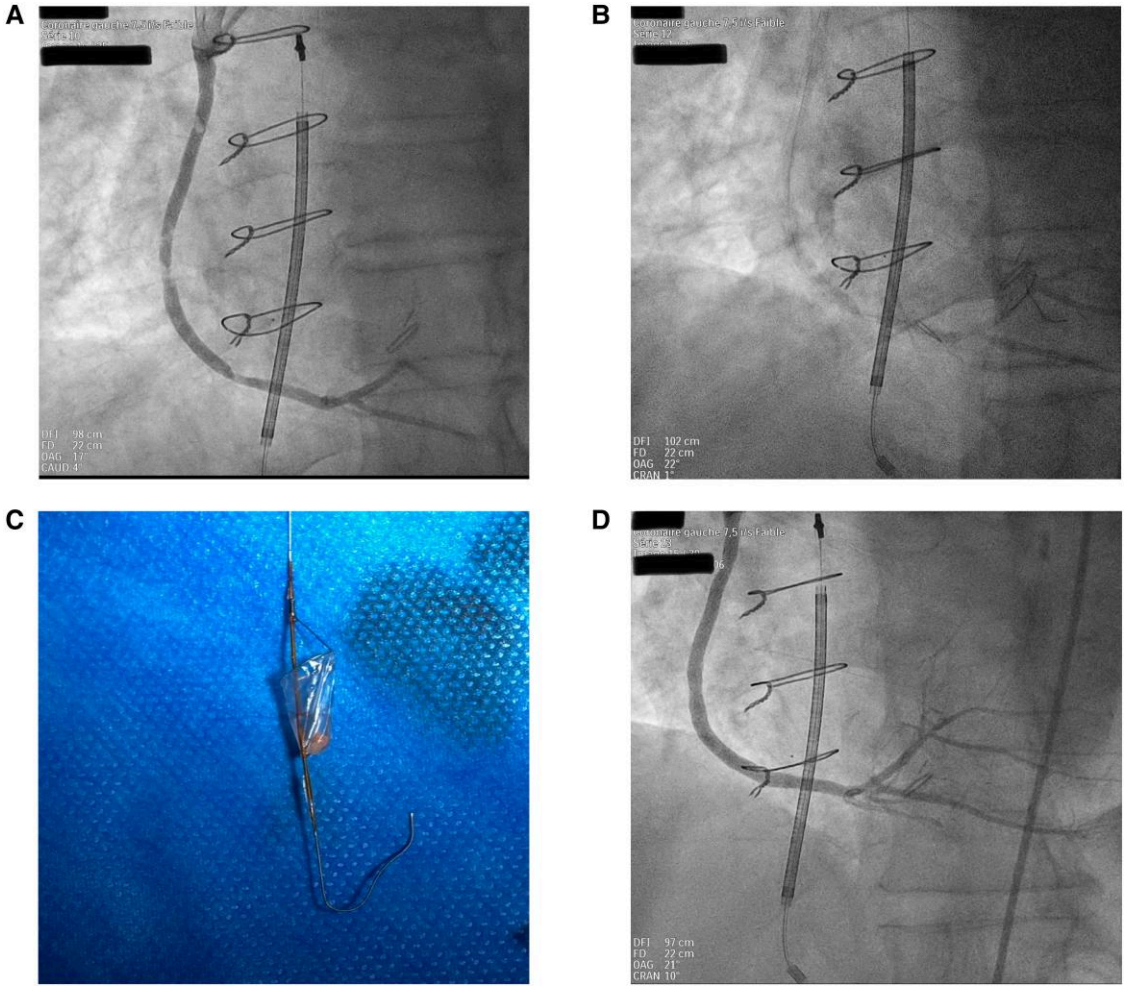


Figure 2 (*A*) Angiographic view of the culprit saphenous vein graft at first presentation with highly thrombotic severe sequential stenosis. (*B*) Deployment of the distal embolic protection device at the distality of the saphenous vein graft. (*C*) Distal embolic protection device after retrieval with significant amount of thrombi trapped inside. (*D*) Angiographic view of the vessel after two stents implantation.

Establishing flow to the SVG was not sufficient because the underlying cause of ST remained unidentified with risk for thrombus reformation. After reviewing the patient's medical records, the daily intake of carbamazepine for epilepsy treatment was noted. Serious interaction of carbamazepine with ticagrelor leads to reduction of plasma ticagrelor levels and was identified as the probable cause of ST. Platelet function tests are not available routinely in our centre, and ticagrelor was switched to prasugrel (loading dose of 60 mg followed by daily maintenance dose of 10 mg). The patient was discharged 5 days later. At 6-month follow-up, he remained free of events with stable and preserved left ventricular function.

Discussion

This case illustrates an overlooked cause of subacute SVG ST leading to acute coronary syndrome and circulatory compromise. Despite optimal stent implantation and compliance to the antiplatelet therapy, a disregarded ticagrelor interaction led to suboptimal platelet inhibition.

Stent thrombosis is related to high mortality reaching 45% and a recurrence rate of 15–20% within 5 years.[2] To minimize risk, optimal stent expansion and apposition verified by intravascular imaging, adequate antiplatelet inhibition, and patient adherence are important.[4] In our case, the patient was under double antiplatelet therapy with aspirin and ticagrelor, and compliance was validated. Optical coherence tomography was used as the preferred modality for in-stent restenosis and ST, due to higher spatial resolution and better tissue characterization than intravascular ultrasound.[5] The previously implanted stent was well apposed and well expanded with no identification of edge dissection or tissue protrusion; thus, the new thrombotic event could not be initially explained. Of note, OCT performance after balloon dilatations may hide possible malposition and underexpansion of the balloon-dilated part. In this case, the occluded part of the vessel only was dilated, and whole stented part was interrogated.

Another aspect of the case's complexity is the SVG PCI. Despite the rapid atherosclerotic progression and the high rate of early SVG occlusion, they are still used in most multivessel aortocoronary bypass surgeries. Failure rate of SVG reaches 8–25% in 1 year and 50–60% after a decade.[6] Moreover, SVG stenting in the context of acute myocardial infarction carries an increased risk of distal embolic phenomena, and protection devices may be considered. In our case, white and red thrombi were retracted from the filter basket, preventing distal

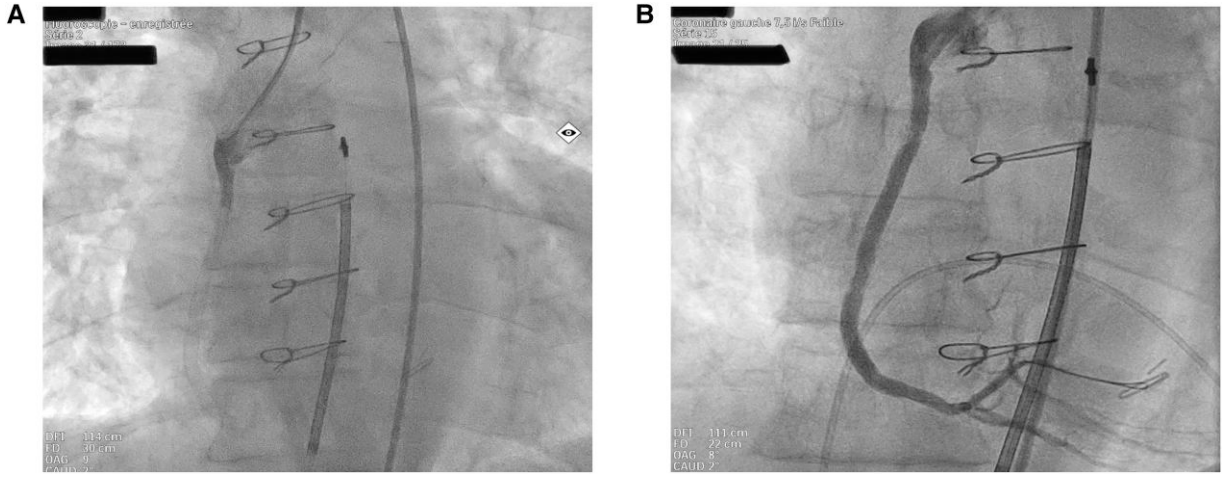


Figure 3 (*A*) Angiographic view showing acute thrombosis of the saphenous vein graft stent and complete occlusion of the flow from the proximal segment. (*B*) Post-balloon angioplasty view with flow restoration and in-stent thrombotic remnants.

embolism and flow limiting complications after PCI. The setting of the subacute ST, however, was accompanied with cardiogenic shock, and the protection device insertion, which can be time consuming, was omitted. Balloon angioplasty removed the occlusive thrombi and restored TIMI 3 flow to the SVG without the use of thromboaspiration, which however could have been considered despite conflicting outcome data.[7,8]

Double antiplatelet treatment is the cornerstone of myocardial infarction and PCI medical treatment and essential to prevent atherothrombotic events and preserve stent intactness. Platelet reactivity tests have been proposed to screen for impaired response to pharmaceutical platelet inhibition.[9] In the presence of genetic polymorphisms, clopidogrel can result in incomplete platelet inhibition. In contrast, the action of ticagrelor that is not a prodrug and does not undergo metabolic activation remains unaffected; however, serious drug interactions have been described.[10] Ticagrelor is metabolized by cytochrome P450 (CYP)3A/CYP2C19 to the active metabolite AR-C124910XX before excretion.[11] Carbamazepine is a potent CYP3A4 inducer and, when coadministered with ticagrelor, increases its clearance and reduces platelet inhibition. Our patient was receiving chronic treatment with carbamazepine for epilepsy that led to reduction of ticagrelor's potency. Prasugrel is a prodrug but has less potential for drug interactions, and after substitution, the patient is event free for 6 months. The metabolic effects are exerted through an active metabolite that undergoes subsequent activation from CYP. However—unlike clopidogrel—trials have shown that prasugrel's clinical effects are not affected by inducers or inhibitors of the P450 system, nor by genetic polymorphisms.[12,13] In a large observational registry, 25% of patients receiving ticagrelor for acute coronary syndrome were taking at least one potentially interacting drug, highlighting the importance of careful scrutinization of the prescribed medication before initiating any regimen.[14] Besides antiplatelet switch, inhibition of factor Xa with rivaroxaban has been proven to be effective in acute coronary syndromes but associated with increased major bleeding risk.[15] This case underlines the perils of polypharmacy and the importance of tailored antiplatelet therapy.

Conclusion

This case report describes a subacute ST secondary to insufficient platelet inhibition due to a ticagrelor–carbamazepine interaction. Identifying the cause of ST is of importance and should be pursued by studying the procedural outcomes with intravascular imaging and scrutinizing patient's history. In this case, an overlooked drug interaction was identified, and ticagrelor was switched to prasugrel to ensure potent platelet inhibition.

Lead author biography

My principal area of interest is interventional cardiology with a focus on percutaneous coronary interventions and structural heart disease interventions. I have obtained my medical degree in the Aristotle University of Thessaloniki and continued my academic education with MSc degree in 2019 and PhD degree in 2023. I have been trained as a cardiology resident in the Athens Naval Hospital and the First Cardiology Department of the University of Athens in Greece. Currently, I am serving as an interventional cardiology fellow at CHU Saint-Pierre, Brussels, Belgium.

Supplementary material

Supplementary material is available at *European Heart Journal – Case Reports* online.

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Consent: Written consent for submission and publication of this case report, including images, was obtained from the patient in accordance with Committee on Publication Ethics (COPE) guidelines.

Conflict of interest: None declared.

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Data availability

The data underlying this article are available within the article.

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