

A Case Report of Ticagrelor-Induced Thrombocytopenia

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Introduction: We report a case of new-onset thrombocytopenia following administration of a loading dose of ticagrelor.

Case Presentation: A 66-year-old male known to have diabetes mellitus type II, chronic obstructive airway disease, and hypertension presented to the emergency department with retrosternal chest pain and dyspnea. Work-up on presentation showed Hb 14.7 g/dL, platelet $229 \times 10^9/L$, and troponin 309 ng/mL. The electrocardiogram showed ST elevation in the anterior-lateral leads. The patient underwent balloon angioplasty, and a drug-eluting stent was deployed. During the procedure, intravenous unfractionated heparin and a 180 mg loading dose of ticagrelor were given. Six hours post procedure, the platelet count was $70 \times 10^9/L$ without active bleeding. Blood smear was unremarkable, and no schistocytes could be seen. So, ticagrelor was stopped, and the patient's platelet count completely recovered four days after discontinuation.

Conclusion: Ticagrelor-induced thrombocytopenia is a rare but increasingly recognized entity. Therefore, post-treatment monitoring and early recognition are crucial parts of management.

Keywords: ticagrelor, thrombocytopenia, coronary artery disease

Introduction

Coronary artery disease (CAD) is one of the leading causes of death worldwide.¹ It has a wide spectrum of angiographic pictures that is translated into a different clinical presentation for each patient. Understanding its pathophysiology has led to reduced mortality through different medical and surgical therapeutic options based on the disease's severity and clinical presentation.² Antiplatelet agents are considered a mainstay of treatment in both its acute and chronic settings. However, the presence or development of thrombocytopenia predicts significantly worse outcomes and has hugely influenced administration of these agents.^{3,4} There are several causes of thrombocytopenia, but the administration of certain medications is one of the most common.⁵ Herein, we report on a case of new-onset thrombocytopenia following administration of a loading dose of ticagrelor.

Case Presentation

A 66-year-old male known to have diabetes mellitus type II, chronic obstructive airway disease, and hypertension presented to the emergency department with severe retrosternal chest pain and progressive shortness of breath. His physical examination was unremarkable apart from oxygen saturation of 91–92% on room air, BP 220/120 mmHg, and tachycardia with a pulse rate of 120 beats/minute.

Initial work-up prior to intervention showed Hb 14.7 g/dL, platelet $229 \times 10^9/L$, troponin 309 ng/mL, PTT 32 seconds, and creatinine 0.9 mg/dL. Furthermore, the 4T-score of our patient was low; therefore, testing for a heparin-induced thrombocytopenia (HIT) antibody panel was not pursued. An electrocardiogram showed ST elevation in the anterior-lateral leads and reciprocal ST depression in the inferior ones. Further, an echocardiography showed a reduced ejection fraction of 45% and left anterior descending artery (LAD) territory hypokinesia. As a bridge to percutaneous

coronary intervention (PCI), the patient received aspirin and beta-blockers as part of an initial anti-ischemic measure in addition to intravenous nitroglycerin to control hypertension.

On the coronary angiography prior to stent placement, total thrombotic occlusion of LAD at its midsegment was seen, along with 30% stenosis of the left circumflex artery (LCX) followed by subtotal occlusion after giving obtuse marginal artery (Figure 1). Therefore, balloon angioplasty was performed, and a drug-eluting stent was deployed (Figure 2). During the procedure, intravenous unfractionated heparin and a 180 mg loading dose of ticagrelor were given. The patient was to be maintained on ticagrelor plus aspirin; however, the platelet count 6 hours post procedure was done as per hospital protocol and revealed a platelet count of $70 \times 10^9/L$ on two occasions with no active bleeding. The peripheral

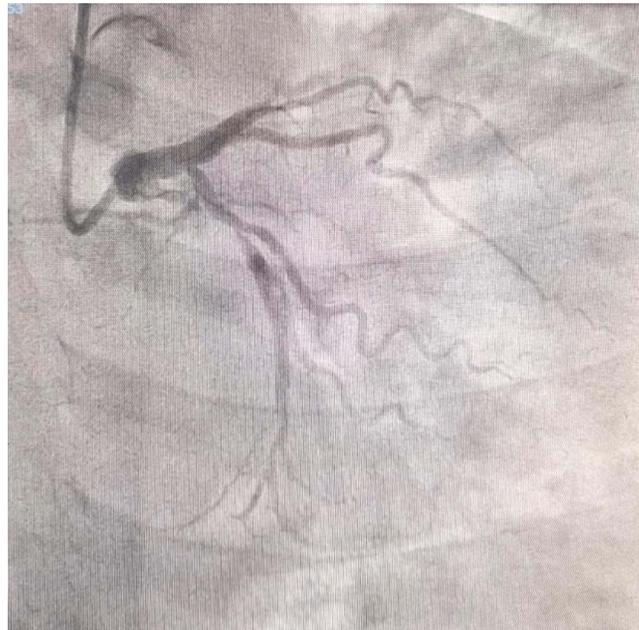


Figure 1 Total thrombotic occlusion of left anterior descending artery and stenosis of the left circumflex artery.

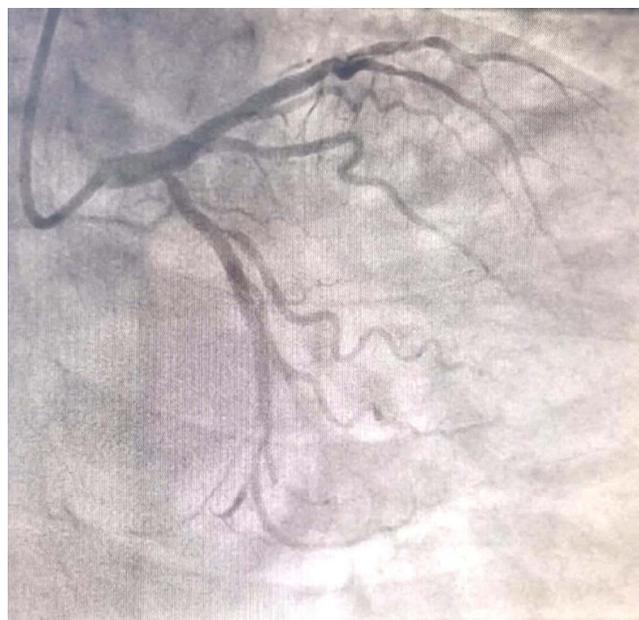


Figure 2 Coronary blood flow after aspiration thrombectomy and balloon angioplasty.

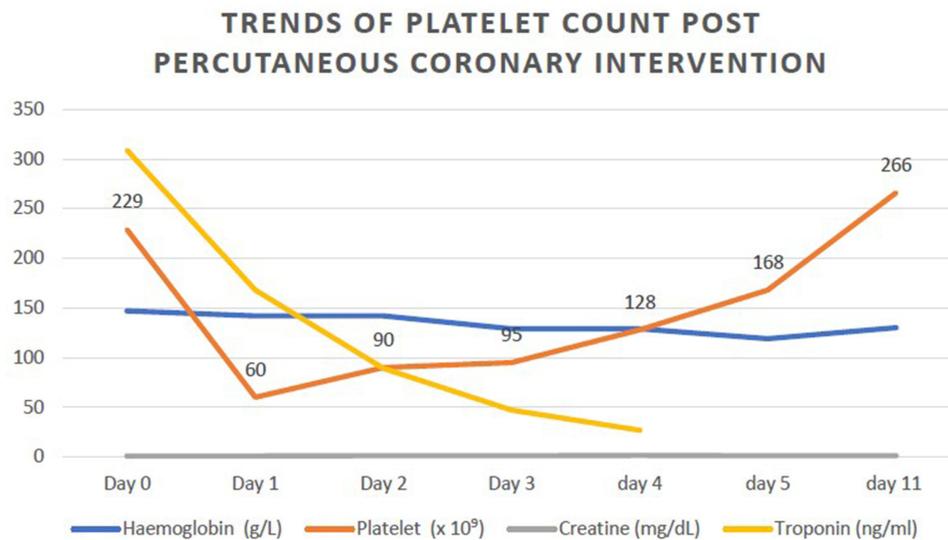


Figure 3 Trends of platelet count post percutaneous coronary intervention.

blood smear was unremarkable, and fragmented red blood cells could not be seen. Additionally, other laboratory parameters including hemoglobin and creatine were within normal ranges and comparable to the baseline line which makes the possibility of microangiopathic hemolytic anemia less likely (Figure 3). We attributed the platelet drop to ticagrelor. Therefore, an additional dose was withheld, and the patient was placed on both aspirin and clopidogrel instead twelve hours following the initial loading dose of ticagrelor. Fortunately, the patient's platelet count recovered gradually, with complete resolution four days after the initial presentation, reaching $168 \times 10^9/L$ without need for a blood component transfusion or other supportive measures, and he was discharged thereafter (Figure 3).

Discussion

Platelets are a fundamental component in the hemostatic system and play an important role in cardiovascular disease pathogenesis.¹ However, antiplatelet therapy reduces the risk of stent thrombosis at the cost of an increased bleeding risk. Therefore, management of acute coronary syndrome in the context of thrombocytopenia is more challenging.^{2,3} Ticagrelor is a potent and direct-acting oral antagonist of the adenosine diphosphate (ADP) receptor P2Y₁₂. It is rapidly absorbed with a median time to peak concentration of two to three hours, and the mean elimination time for ticagrelor and its metabolites is seven to nine hours, respectively.⁶ Several guidelines recommend it over other antiplatelet agents based on platelet inhibition and patients' outcome trials, though major bleeding remains a concern.^{7,8}

In our report, the patient developed thrombocytopenia following administration of a loading dose of ticagrelor which augmented the patient's risk of bleeding. However, early recognition prompted rapid discontinuation of ticagrelor, resulting in the subsequent gradual improvement of platelet count. To our knowledge, this is the fifth report of ticagrelor-induced thrombocytopenia and the second with thrombocytopenia developing in as early as 6 hours.⁹ In contrast, thrombocytopenia in previous cases presented at 4 to 14 days post administration of ticagrelor.^{5,10,11} Of note, only our report reveals complete recovery of platelet count upon discontinuation of ticagrelor, whereas other patients required various additional treatments, including steroids, plasma exchange, and platelet transfusion.^{5,9-11} Rechallenge with suspected drug causing thrombocytopenia though is not definite, but it is another way of proven causation.¹² However, rechallenge was not considered in our patient given his serious cardiac disease.

Heparin-induced thrombocytopenia is an important differential diagnosis for thrombocytopenia in our patient since he was exposed to heparin, but the possibility was low as he had low 4T-score. Additionally, past medical history for him is significant for heparin exposure, but no thrombocytopenia was documented. Similarly, type I heparin-induced thrombocytopenia would lead to acute thrombocytopenia irrespective of 4T-score; however, platelet count is expected to drop

within two days of exposure to heparin, with a nadir platelet count usually $100 \times 10^9/L$ and above which is not the case here.¹³

Ticagrelor-induced thrombocytopenia is rare; however, this and previous reports indicate that it is an increasingly recognized entity. Despite that, the mechanism of ticagrelor-induced thrombocytopenia has not yet been determined. Moreover, there are no clear indicating factors for which individuals will develop it compared to others, though sex may be a factor as it was observed more among males.

Furthermore, this report highlights the importance of testing for platelet count as early as 6 hours post treatment as this will be necessary for subsequent antiplatelet choice of treatment, avoidance of unwanted bleeding, and unnecessary blood component transfusion.

In conclusion, ticagrelor-induced thrombocytopenia is a rare side effect, and its presence may augment bleeding risk and reshape treatment plan of coronary artery disease. Therefore, post-treatment monitoring and early recognition are crucial and should be incorporated into future management protocols.

Ethical Approval

Institutional approval is not required for publication, so informed written consent for using patient information and case report publication was obtained from the patient as long as identifying data are anonymous.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The author declares no conflicts of interest in this work.

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