ISSN: 2634 - 6796

Journal of Cardiology Research Reviews & Reports

SCIENTIFIC Research and Community

Case Report

Open Access

Tirofiban-Induced Severe Thrombocytopenia Post-Drug Eluting Balloon Coronary Intervention: A Case Report

Kashif Bin Naeem[1]* and Abdalla Alhajiri[1]

1Al Kuwait Hospital, Dubai, Ministry of Health and Prevention, UAE

ABSTRACT

Background: Glycoprotein IIb/IIIa inhibitors have been reported to cause thrombocytopenia, however, only few case reports exist regarding tirofiban. We report a rare case of tirofiban-induced severe thrombocytopenia and its management.

Case Presentation: We present a 51-year-old male who underwent coronary angioplasty with drug eluting balloon for exertional angina. The platelet count dropped from 230 x 10^9/L (before angiogram) to 3.8 x 10^9/L within 24 hours of intravenous tirofiban infusion without active bleeding. We transfused 4 units of platelets, continued aspirin and clopidogrel and monitored in coronary care unit. Gradually the platelet count improved with no evidence of bleeding, ischemic or thrombotic events.

Conclusion: The case highlights the awareness for the dramatic and profound tirofiban-induced thrombocytopenia that may pose a challenge to manage.

***Corresponding author**
Kashif Bin Naeem, Al Kuwait Hospital, Dubai, Ministry of Health and Prevention, UAE; Tel: +971 569443145. E-mail: kbncardiology@yahoo.co.uk

Received: November 29, 2020; **Accepted:** December 04, 2020; **Published:** December 15, 2020

Keywords: Case Report, Tirofiban, Thrombocytopenia, Drug-Eluting Balloon, Coronary Intervention.

Abbreviations
GP IIb/IIIa inh: Glycoprotein IIb/IIIa inhibitors
ECG: Electrocardiograph
CBC: Complete Blood Count
TIMI: Thrombolysis in Myocardial Infarction

Background

Glycoprotein IIb/IIIa inhibitors (abciximab, eptifibatide, tirofiban), potent intravenous anti-platelet medications, are currently being used in the treatment of acute coronary syndromes, with proven benefit in patients undergoing percutaneous coronary intervention [1]. Although all the three drugs in the group have been associated with thrombocytopenia, abciximab carries higher risk compared to other medications while only few cases have reported severe thrombocytopenia with tirofiban [2]. The cases reported have been related to coronary stenting. Hence, we report a rare case who developed profound thrombocytopenia after intravenous administration of tirofiban during the coronary intervention with drug-eluting balloon and highlight its management.

Case Presentation

History

A 51-year-old Syrian gentleman, known hypertensive and dyslipidemic, was seen in the cardiology out-patients where he reported worsening effort angina with shortness of breath. Cardiovascular examination was unremarkable. Electrocardiography (ECG) showed sinus rhythm with no acute ST-T wave changes. Transthoracic echocardiography showed normal left ventricular size and wall motion. He underwent exercise ECG test that revealed significant exercise-induced ischemic ECG changes.

The Intervention

The patient was subsequently admitted for coronary angiography. On the day of admission, before the angiogram, his blood tests showed hemoglobin 15 g/dl, white cell count 6 x 10^9/L and platelets 230 x 10^9/L. The rest of blood tests including renal functions, liver functions and coagulation profile were all normal. The sample for complete blood count (CBC) was collected in tubes containing EDTA (Ethylene diamine tetra acetic acid) as an anticoagulant and the tests were performed using Siemens Advia 2120i hematology analyzer. He was given aspirin 300 mg and clopidogrel 600 mg orally before the angiogram. The coronary angiogram was performed via right radial artery approach. A 5F TIG catheter was used. This showed unobstructed left main artery, with mild plaques in left anterior descending artery, left circumflex artery and right coronary artery without significant obstruction. However, a branch of ramus intermedius had 80% stenosis in mid-vessel and it was decided to proceed with angioplasty. As the diseased vessel was small (2 mm), it was decided to treat with a drug-eluting balloon in place of a stent. 6F EBU 3.0 guiding catheter with 0.014 BMW wire was used to access the lesion that was then predilated with 2x10 mm Sequent Neo (B Braun) at 12 atmospheres. This was followed by deployment of 2x20 mm

Sequent Please Drug Eluting Balloon at 6 atmospheres, resulting in TIMI 3 flow (Figure 1). A total of 8000 units of intracoronary heparin was given during the procedure only. Intravenous tirofiban was commenced during the procedure and continued for 24 hours at a dose of 0.4 mcg/kg/min for 30 minutes followed by 0.1 mcg/kg/min for 24 hours. The procedure went uncomplicated.

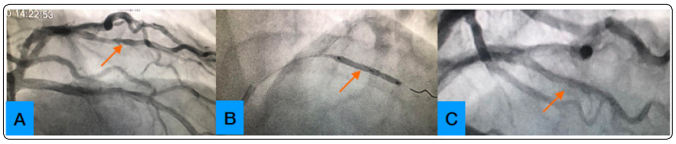

Figure 1: Coronary angiogram showing the right anterior oblique views.
Arrow in [A] indicates the lesion in Ramus branch, followed by insertion of drug eluting balloon (arrow in [B]). [C] shows post-intervention view with TIMI III flow in the treated vessel.

Post-Intervention

Complete blood count was repeated next day after the intervention as a routine. The platelet count had reduced dramatically to 4.8 x 10^9/L (compared to 230 x 10^9/L before the intervention). Hemoglobin was normal, 13.8 g/dl. The patient felt fine with no signs of active bleed. A repeat test after 4 hours showed platelet count drop to 3.8 x 10^9/L (Figure 2). Hemoglobin was 14.4 g/dl and white cell count 11.7 x 10^9/L. We requested a manual platelet count by visual inspection of the hematological blood smear under microscope that confirmed the result of the automated CBC test and did not show any platelet clumping. The patient was immediately transferred to the coronary care unit and monitored closely. We continued aspirin and clopidogrel due to the high risk of stent thrombosis. Although the patient showed no signs of active bleed, he was transfused with 4 units of cross-matched platelets in view of very low platelet count. Repeat test next day showed platelet count improved to 40 x 10^9/L. The patient did not have any bleeding, ischemic or thrombotic events during the hospital stay and was discharged next day, when repeat test showed platelet count of 60x 10^9/L.

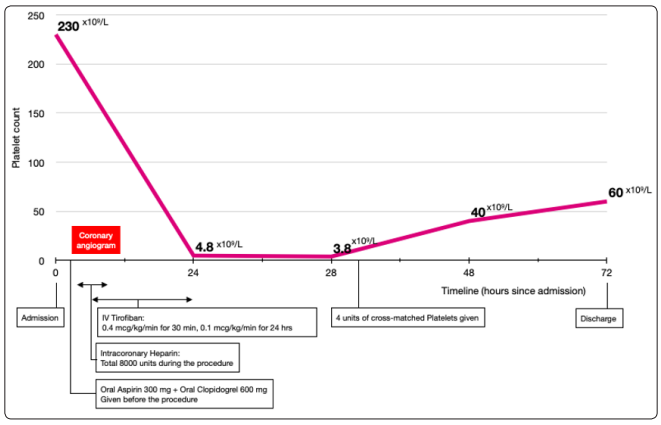

Figure 2: Platelet count over time with relation to drug exposure

Follow Up

He was reviewed in the out-patient clinic one week after discharge. He did not report any ischemic symptoms. A repeat CBC showed hemoglobin 14.8 g/dl, white cell count 6.3 x 10^9/L and platelet count 257 x 10^9/L.

Discussion

We present a rare case of tirofiban-induced thrombocytopenia after treating a coronary artery stenosis with a drug-eluting balloon. The case is unique as there are no cases reported earlier following a drug-eluting balloon.

The human Glycoprotein IIb/IIIa belongs to a family of cation-dependent adhesion molecules (known as integrins) that mediate the final common pathway of platelet aggregation. GP IIb/IIIa inhibitors, antagonists to this receptor, compete with fibrinogen and von Willebrand factor for binding to this receptor, and thus interfere with platelet cross-linking and subsequent thrombus formation with very potent anti-platelet activity. Three drugs from this group are approved for clinical use: abciximab, tirofiban and eptifibatide. These agents were in popular use during the plain balloon angioplasty era to reduce post-procedure stent thrombosis [3]. However, their use has decreased since the introduction of oral P2Y12 inhibitors. In the setting of unstable angina (as our patient), these agents have proven benefit mainly for patients undergoing coronary intervention [4].

Thrombocytopenia has been reported with the use of all GP IIb/IIIa inhibitors (abciximab, tirofiban and eptifibatide). The reported incidence of thrombocytopenia is highest with abciximab (2.4%) compared to tirofiban (0.5%) and eptifibatide (0.2%). It usually takes 24 hours to develop severe thrombocytopenia and the platelets may take 1-6 days to return to normal [5]. The exact mechanism is unclear, however, likely considered to be immune-mediated [6]. The differential diagnoses of acute thrombocytopenia in our patient included pseudo-thrombocytopenia, heparin-induced or tirofiban-induced thrombocytopenia. Pseudo-thrombocytopenia is the term used to define a false-low platelet count due to platelet clumping that may occur in the EDTA specimen tube. This was ruled out by manual visual counting of platelets in the peripheral blood smear under the microscope. Although enzyme-linked immunosorbent assay to detect anti-heparin-PF4 antibodies is recommended to diagnose heparin-induced thrombocytopenia, the test was not available at our center. We concluded tirofiban as the likely cause of thrombocytopenia due to its rapid onset after the tirofiban infusion.

The principles of treatment depend upon the severity of thrombocytopenia and the presence of bleeding [7]. Once platelet count is less than 100 x 10^9/L, true thrombocytopenia should be confirmed and potential etiologies be looked into. In general, the GP IIb/IIIa inhibitor should be discontinued, patient should be careful monitored in coronary care unit, and consider platelet transfusion once the count drops to less than 10 x 10^9/L, even in the absence of active bleeding. Intravenous immunoglobulin G has also been used in few instances of tirofiban-induced thrombocytopenia with active bleeding [8]. In our case, we discontinued tirofiban, however, we continued aspirin and clopidogrel due to high risk of acute stent thrombosis. No further heparin was given. Although the patient did not have any signs of active bleed, we decided to transfuse 4 units of cross-matched platelets as the count was too low (3.8 x 10^9/L).

This case, thus, illustrates a very rare episode of severe thrombocytopenia after tirofiban administration and creates awareness of this complication with GP IIb/IIIa inhibitors for the interventional cardiologists.

Conclusion

Intravenous tirofiban-induced thrombocytopenia is rare but can be profound and challenging to manage. We report a rare such case post drug-eluting balloon coronary intervention. The drop in platelet count can be sudden and dramatic, and such patients need to be closely monitored in a coronary care unit to provide

treatment and early identify ischemic, thrombotic and bleeding events if any.

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