



# Tirofiban Induced Severe Thrombocytopenia with Spontaneous Recovery

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## Abstract

GPIIb/IIIa inhibitors (e.g., Tirofiban, abciximab, and eptifibatid) are associated with rapid onset thrombocytopenia, occurring within minutes to hours after exposure. This is an intriguing case of Tirofiban-induced thrombocytopenia with platelet count dropping from  $254 \times 10^3/\text{uL}$  at baseline to  $4 \times 10^3/\text{uL}$  in 12 h after initiation of Tirofiban infusion. The drug was immediately discontinued and platelet count recovered quickly and spontaneously, reaching the normal range within the following 24 h. This case of Tirofiban-induced thrombocytopenia emphasizes the importance of regular platelet count monitoring when administering GPIIb/IIIa inhibitors especially tirofiban and the importance of recognizing and promptly managing such complications in the hospital setting.

**Keywords:** Thrombocytopenia; Platelet dysfunction; Antiplatelet therapy; GPIIb/IIIa inhibitors; Tirofiban

## Case Summary

A 65-year-old male presented to the hospital ER with acute onset chest pain starting approximately 45 min prior to arrival. The patient was a former smoker who quit 30 years ago. Testing revealed anterior wall ST elevation myocardial infarction on EKG. He was given 325 mg Aspirin, Brilinta 180 mg, 4000 units of IV heparin, and was emergently taken to the cardiac catheterization lab for further work up. The results revealed an ostial-proximal LAD lesion with a filling defect suggestive of thrombus, and successful PCI was done with 3.0 mm  $\times$  20 mm Synergy stent and the patient was started on IV Tirofiban infusion after a bolus due to the presence of the filling defect. The Tirofiban infusion was continued for approximately 11 h, during which the patient developed multiple petechiae and a blister in his oral cavity that eventually ruptured. His platelet count, 11 h after administering Tirofiban, was found to be  $4 \times 10^3/\text{uL}$  ( $125\text{-}245 \times 10^3/\text{uL}$ ) while his platelet count on admission was  $254 \times 10^3/\text{uL}$ .

A manual review of the peripheral film by the pathologist confirmed severe thrombocytopenia and ruled out pseudothrombocytopenia. A negative result on the Heparin-induced platelet antibody and serotonin release assays, in combination with the absence of prior heparin exposure in the last 6 months, ruled out Heparin Induced Thrombocytopenia (HIT) Type 1 while the sudden drop in platelet count in 12 h made HIT Type II unlikely. Tirofiban infusion was immediately stopped. Platelet counts were monitored every 6 h with gradual improvement in the platelet counts to  $40 \times 10^3/\text{uL}$  in the next 24 h. The patient did not experience any adverse events associated with bleeding nor did they suffer from any hemodynamic instability.

Follow-up after 1 week showed complete resolution of thrombocytopenia with platelet counts improved to  $369 \times 10^3/\text{uL}$  (Table 1).

## Discussion

Tirofiban is a glycoprotein IIb/IIIa inhibitor, which has been demonstrated to be beneficial in the prevention of thrombus formation in medical conditions such as acute coronary syndrome, unstable angina and non-ST-segment elevation myocardial infarction [1]. PRISM-PLUS and ADVANCE studies have evidenced the efficacy of Tirofiban in inhibiting platelet aggregation and reducing ischemic/thrombotic complications [2,3]. Although tirofiban is highly effective at preventing thromboembolic events, it can also cause thrombocytopenia in some patients. Most

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Received Date: 30 Oct 2023

Accepted Date: 10 Nov 2023

Published Date: 15 Nov 2023

### Citation:

Ahmad B, Shaukat T, Rehman W, Muneeb A. Tirofiban Induced Severe Thrombocytopenia with Spontaneous Recovery. *Ann Cardiol Cardiovasc Med.* 2023; 6(1): 1051.

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**Table 1:** Platelet counts at baseline and after initiation of tirofiban infusion.

Sample time	Platelet count (10 <sup>3</sup> /uL)
Baseline	254
12 h	4
18 h	8
24 h	11
30 h	17
36 h	40
48 h	50
1 week	369

cases of tirofiban-associated thrombocytopenia have been transient and resolved with drug discontinuation [2,3]. The onset of tirofiban-induced thrombocytopenia is typically seen within twenty-four hours, but can occasionally occur within thirty minutes to several hours [3].

Clinical trials of Tirofiban have shown that platelet counts of less than  $100 \times 10^3/\text{uL}$  can occur in 1.1% to 1.9% of patients, and counts of less than  $50 \times 10^3/\text{uL}$  can occur in 0.2% to 0.5% of patients [4]. Typically, this drop in platelet counts occurs within 24 h, though it can occur within 30 min to several hours in some cases [3,4].

Nevertheless, previous case reports have not documented such a sudden drop in platelet counts and spontaneous recovery shortly after cessation of Tirofiban, making this case unique.

Drug-dependent antibodies that destroy platelets are thought to be involved in thrombocytopenia secondary to Tirofiban use [5,6]. The antibodies can develop naturally before exposure or are induced by prior exposure to the drug [7]. Multiple studies support the claim that thrombocytopenia seen in humans following glycoprotein IIb/IIIa inhibitors use is immune mediated and due to the action of antibodies [8].

Studies suggest that thrombocytopenia induced by tirofiban is likely related to suppression of platelet aggregation, decreased production of platelets due to inhibition of fibrin and thrombin formation, and potential immunologic reactions. In addition, it has been suggested that this adverse effect is caused by an immune-mediated response where antibodies, both pre-existing and induced by drug exposure, are formed to target and destroy platelets [7].

The management of tirofiban induced thrombocytopenia includes discontinuation of the medication followed by supportive care. If bleeding complications occur, further treatments such as steroids, intravenous Immunoglobulin (Ig-G), and platelet transfusions may be utilized [9].

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