

A Case of Delayed Onset Tirofiban Induced Thrombocytopenia in a Chronic Renal Failure Patient

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ABSTRACT

Compared with heparin induced thrombocytopenia (HIT), glycoprotein (GP) IIb/IIIa inhibitor induced thrombocytopenia is characterized by a rapid and profound fall in the platelet count. In severe cases, the platelet count decreases below $20,000/\text{mm}^3$ within the initial 24 hours after exposure to the drugs. It is often associated with severe bleeding complications. Tirofiban is one of the GP IIb/IIIa inhibitors. A case of severe thrombocytopenia in a 60-year-old man, with chronic renal failure (CRF) and acute myocardial infarction (AMI), was recently experienced. Tirofiban was administered to treat the AMI without ST segment elevation. The platelet count fell to $1,000/\text{mm}^3$ with hemoptysis and petechiae 80 hours after the initiation of tirofiban infusion. In this case, the clinical course was similar to that of the typical GP IIb/IIIa inhibitors induced thrombocytopenia, with the exception that its onset time was unusually delayed. The platelet count was normalized in 9 days after cessation of tirofiban infusion. Thus, this unusual case is reported as delayed onset tirofiban induced thrombocytopenia in a CRF patient. (Korean Circulation J 2004;34(7):715-717)

KEY WORDS : Thrombocytopenia ; Platelet aggregation inhibitor ; Heparin ; Chronic renal failure.

Introduction

Tirofiban is one of the GP IIb/IIIa inhibitors. Recently, we experienced a case of thrombocytopenia in a 60-year-old man with CRF and AMI. The clinical course was similar with typical GP IIb/IIIa inhibitors induced thrombocytopenia except that its onset time was unusually delayed. Thus, we report this unusual case as a delayed onset tirofiban induced thrombocytopenia in a CRF patient.

Case

On January 31, 2003, a 60-year-old man visited our emergency room with squeezing anterior chest pain,

exertional dyspnea (NYHA class III), blood tinged sputum and generalized pitting edema. The patient had ever been diagnosed as Immunoglobulin A nephropathy (IgA nephropathy) and CRF in 1995. Thereafter, he was followed up to the nephrology department without dialysis. In September, 2002, he experienced intermittent chest pain and visited our cardiology department. Treadmill test showed ST segment depressions of 3 mV in inferior leads (II, III and aVF) and coronary angiogram showed a diffuse 3-vessel disease. Percutaneous transluminal coronary angioplasty (PTCA) was done on distal circumflex artery. After PTCA, he was followed up to the cardiology department without cardiac symptoms. However, he revisited our emergency room for the formerly mentioned chief complaints.

On admission, blood pressure was 140/90 mmHg, heart rate 92 beats/minute, respiration rate 26 times/minute and body temperature 36.9°C . Moist rales were heard on both lung fields without cardiac murmurs. Conjunctiva was pale and generalized pitting edema with

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mild neck vein engorgement was observed. In complete blood cell count, hemoglobin was 6.2 g/dL, platelet count $257,000/\text{mm}^3$ and WBC count $13,400/\text{mm}^3$. Cardiac enzymes and other chemistry results were as followings. CK 320 mg/dL, CK-MB 19 U/L, LDH 577 U/L, Troponin-I 4.39 ng/mL (late peak troponin-I was 11.4 ng/mL), BUN/creatinine 109/8.8 mg/dL, PaO₂ 50 mmHg, PaCO₂ 20 mmHg, SaO₂ 88%, pH 7.49. Liver function test results were within normal reference range. Anti-platelet antibody and platelet associated antibodies were not detected. Initial ECG showed ST segment depressions on precordial leads (V3–V5) and pathologic Q waves on limb leads (III and aVF). Chest X-ray showed marked cardiomegaly and increased pulmonary vascular markings of the both lungs. Echocardiography showed ejection fraction 42%, mitral regurgitation (grade II), tricuspid regurgitation (grade I). Hypokinesia of the myocardium was observed in the left anterior descending coronary artery territory.

With the diagnosis of AMI without ST segment elevation, heparin and aspirin were initiated on the 1st hospital day. On the 2nd hospital day, tirofiban was added with dose reduction by 50% because of underlying

CRF. On the 6th hospital day (100 hours after the initiation of heparin infusion and 80 hours after the initiation of the tirofiban infusion), the profound thrombocytopenia with bleeding complications including generalized petechiae and large amount of hemoptysis appeared for the first time. The platelet count fell to the $1,000/\text{mm}^3$ from the $200,000/\text{mm}^3$ of the 5th hospital day in one day. All anti-platelet agents were discontinued immediately. Protamine sulfate was administered and repeated platelet transfusions were done. Nevertheless, severe thrombocytopenia (the platelet count about $1,000/\text{mm}^3$) lasted over 3 days. From the 8th hospital day, repeated hemodialyses were performed to control pulmonary edema and bleeding tendency. The platelet count increased markedly on the next day after the first hemodialysis and normalized on the 13th hospital day (5 days after starting the hemodialysis). The clinical course of the thrombocytopenia is shown in Figure 1.

Discussion

Thrombocytopenia is well known complication of

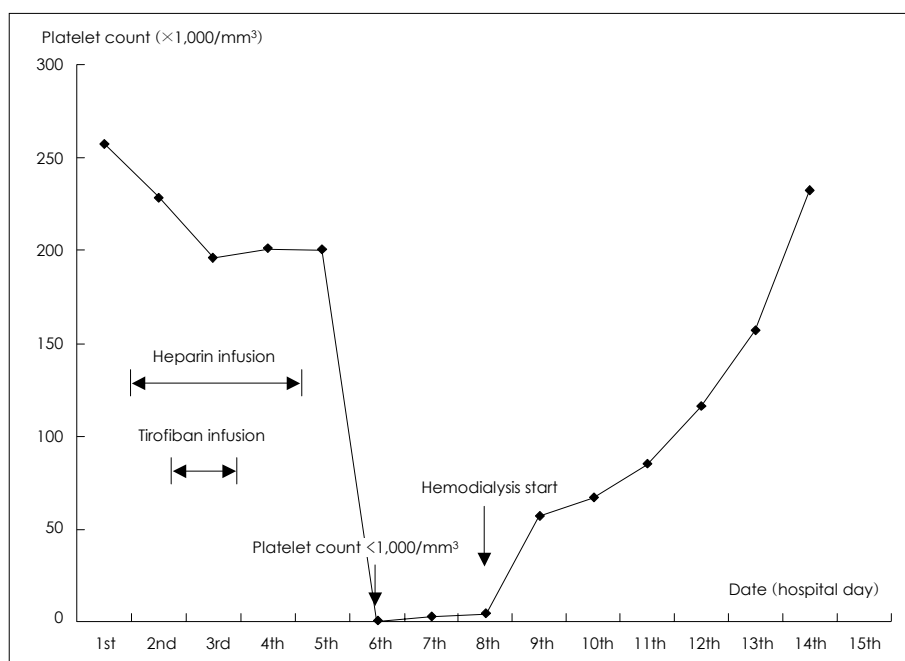


Figure 1. Platelet count and clinical course in delayed onset tirofiban induced thrombocytopenia.

heparin therapy. Type I HIT is non-immune thrombocytopenia and characterized by the mild decrease of platelet count within early two days of heparin administration. The platelet count returns to the normal range with continuous heparin administration without significant bleeding events.^{1,2)} Type II HIT is antibody mediated immune reaction against the heparin-platelet factor 4 complex.³⁾ It is often associated with paradoxical venous or arterial thrombotic events.^{4,5)} In typical cases, it is characterized by the decrease of platelet count in 4 to 10 days after exposure to the heparin.^{3,6)} In some patients who were exposed to the heparin within recent 100 days, rapid onset thrombocytopenia may appear in 2 to 18 hours after re-exposure to the heparin.⁶⁾ However, in both cases, the platelet count rarely falls below 20,000/mm³.

GP IIb/IIIa inhibitors, a new class of antithrombotic agents, were proven effective in reducing major adverse cardiac events after PTCA.⁷⁻⁹⁾ The FDA approved three kinds of GP IIb/IIIa inhibitors; abciximab, eptifibatide and tirofiban for specific conditions in PTCA. In the previous studies with these agents, some cases of severe thrombocytopenia and bleeding complications were reported.¹⁰⁻¹³⁾ GP IIb/IIIa inhibitors induced thrombocytopenia is known as an antibody mediated immune reaction. However, compared with HIT, it is characterized by the acute onset thrombocytopenia within initial 24 hours after exposure to these agents. In severe cases, the platelet count falls below 20,000/mm³ and it is often associated with bleeding events.¹⁴⁾ Recently, we experienced several cases of thrombocytopenia after tirofiban administration. However, in this particular case, the platelet count fell to the 1,000/mm³ with bleeding complications 80 hours after the initiation of tirofiban infusion. Before 4 months, he was exposed to the heparin due to previous PTCA but not tirofiban. Because antibodies to the heparin or tirofiban were not examined in this patient, we could not mention exactly which antibody induced this severe thrombocytopenia. However, the clinical course was similar with the typical tirofiban induced thrombocytopenia except that its onset time was markedly delayed. Thus, we report a case of delayed onset thrombocytopenia in a

CRF patient. We guess that the thrombocytopenia of abnormal clinical course in this patient might be affected by underlying IgA nephropathy or CRF. Although the platelet count increased remarkably after hemodialyses. It is also unclear whether the recovery of thrombocytopenia had causative relationship with hemodialysis or not.

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