CASE REPORT

Abciximab-induced acute profound thrombocytopenia postpercutaneous coronary intervention

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SUMMARY

Abciximab (c7E3 Fab) is one of the three potent intravenous glycoprotein IIb/IIIa receptor inhibitors (along with eptifibatide and tirofiban) that have shown significant positive outcomes when used in patients with intracoronary thrombus. However, major side effects have been reported with its use including hypotension, major bleeding and thrombocytopenia. This case is a 53-year-old man presenting with acute chest pain diagnosed with non-ST-elevation myocardial infarction, who underwent percutaneous coronary intervention with abciximab and heparin infusion and developed acute profound thrombocytopenia (platelet count <20,000/L) within 9 hours of infusion. This case demonstrates the importance of routinely monitoring the platelet count prior to and 2–4 hours following abciximab infusion and differentiating other causes of acute profound thrombocytopenia, particularly pseud thrombocytopenia and heparin-induced thrombocytopenia.

BACKGROUND

We present a rare (<1%) complication of acute profound thrombocytopenia following percutaneous coronary intervention with abciximab, in a male patient with non-ST segment elevation myocardial infarction. We also review the clinical considerations of this idiosyncratic complication. Although profound thrombocytopenia is recognised as a serious complication of abciximab, this case is noteworthy due to its extreme rarity and the successful outcome.

CASE PRESENTATION

A 53-year-old man on warfarin with a history 12 years prior of prosthetic aortic valve replacement (AVR) secondary to endocarditis presented to the emergency department with chest pain. Vital signs revealed a temperature of 36.5°C, pulse of 64/min, blood pressure of 134/88 mm Hg, respiratory rate of 16/min and oxygen saturation of 100%. His weight was 72 kg. He was alert, awake and oriented to person, place and time. The jugular venous pressure was elevated to 6 cm. Cardiac exam showed normal sinus rhythm with audible mechanical valve click, and there was no chest wall tenderness on palpation. The lungs were clear to auscultation bilaterally. Lower extremities were normal without oedema. The complete blood count was normal with a white cell count (WCC) of 7.5/L, haemoglobin of 14.5 g/dL and platelet count of 155×1000/L. Comprehensive metabolic profile

was normal with the exception of a sodium level of 132 mmol/L. International normalised ratio was 1.6 and prothrombin time was 19.7 s. Troponin level on initial presentation was 0.08 ng/mL. An ECG done in the emergency department showed normal sinus rhythm with left axis deviation. CT angiography of the chest was negative for pulmonary embolism, dissection or aneurysm. Echocardiogram showed left ventricular ejection fraction of 55% with mild lateral wall hypokinesis. Thyroid stimulating hormone was normal, haemoglobin A1c was 6% and the lipid profile was normal with the exception of a triglyceride level of 214 mg/dL (normal <149 mg/dL). Given his AVR history, he was admitted to the cardiac care unit with concern of non-ST elevation myocardial infarction. Acute coronary syndrome protocol was started in the emergency department with 325 mg aspirin orally and initiation of an intravenous heparin drip. During his hospital stay, the patient continued to be free of chest pain and the ECG remained unchanged from the initial ECG obtained in the emergency department. However, his troponin gradually peaked to 29.22 ng/mL within 30 hours. After discussing the risks and benefits of cardiac catheterisation with the patient and obtaining his consent, the patient underwent percutaneous coronary intervention (PCI) which found a thrombus in the ramus intermedius, and a single dose of 18 mg (0.25 mg/kg) abciximab was given intracoronary followed by aspirational thrombectomy. A resolute drug-eluting stent 2.25 mm by 18 mm was deployed. The patient tolerated the procedure well without complications. Post-PCI, the patient was started on clopidogrel 75 mg and aspirin 81 mg daily. His blood pressure and heart rate remained within normal levels throughout the day. Nine hours following PCI, his blood workup showed profound thrombocytopenia with platelet count of only 3×1000/L, haemoglobin of 14.6 g/dL and WCC of 6.1/L. A re-collection of blood sample using sodium citrate confirmed thrombocytopenia. Heparin was discontinued. Heparin-induced thrombocytopenia (HIT) was negative. The patient was asymptomatic with normal vital signs. He was transfused a total of one apheresis platelet (6 units of platelets). On checking his platelet count post-transfusion, it increased to 25×1000/L. The patient was closely monitored for any signs of bleeding and thrombosis; however, none were exhibited. His platelets continued to trend upward and he was discharged 3 days after the initial thrombocytopenia with a platelet count of 62×1000/L. Warfarin therapy was reinitiated inpatient, when

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platelets count reached above $50 \times 1000/\text{L}$. At follow-up 10 days postdischarge, the patient reported walking about a mile without shortness of breath or chest pain, and his platelets were up to $366 \times 1000/\text{L}$, indicating recovery from abciximab-induced thrombocytopenia and remained normal at 1 week follow-up.

INVESTIGATIONS

A blood sample re-collection using sodium citrate confirmed thrombocytopenia. HIT was negative.

DIFFERENTIAL DIAGNOSIS

- ▶ HIT: less likely given the timing of thrombocytopenia.
- ▶ Pseudothrombocytopenia: differentiated using peripheral smear or repeat platelet count with citrate anticoagulated blood.

OUTCOME AND FOLLOW-UP

At follow-up 10 days postdischarge, the patient reported walking about a mile without shortness of breath or chest pain, and his platelets were up to $366 \times 1000/\text{L}$, indicating recovery from abciximab-induced thrombocytopenia, and platelets remained normal 1 week later.

DISCUSSION

Abciximab, a glycoprotein IIb/IIIa receptor inhibitor, is a potent antiplatelet agent that blocks the final pathways to platelet aggregation. It is effective in preventing and treating acute ischaemic complications of percutaneous coronary intervention and is well established in improving the outcomes of high-risk procedures by decreasing the incidence of major adverse cardiac events.^{1–3} Consequently, it is recommended as adjunctive therapy to PCI by the American College of Cardiology, American Heart Association and European Society of Cardiology guidelines. Thrombocytopenia following percutaneous coronary intervention represents a rare and clinically challenging complication associated with a haemorrhagic risk of major concern.^{3,4} Risk factors for thrombocytopenia include age >65 years, weight <80 kg and a baseline platelet count $<200\,000/\text{L}$, with the number of these three risk factors increasing the thrombocytopenia incidence ((0) 1.8%, (1) 2.3%, (2) 8.0%, (3) 9.8%).⁵ Our patient had two of these three risk factors, with a weight of 72 kg and a baseline platelet count of $155\,000/\text{L}$. Abciximab-induced acute profound thrombocytopenia (platelet count of $<20\,000/\text{L}$) represents a rare, unpredictable, serious adverse complication, capable of causing fatal haemorrhagic events including intracranial haemorrhage.^{6–8} Additional thrombocytopenia complications include increased risk of death, myocardial infarction, bypass surgery, additional percutaneous revascularisations and balloon pump insertions, longer duration of stay in the coronary care unit and increased risk of bleeding.^{5,9} In clinical trials, as well as in clinical practice, $<1\%$ of patients receiving abciximab experience acute profound thrombocytopenia; in fact, three studies, totalling >1700 patients, have demonstrated this rare complication has an incidence $<0.7\%$ (0.53%, 0.6% and 0.66%).^{10–15} We report a case of acute profound abciximab-induced thrombocytopenia and its successful management, treatment with abciximab discontinuation and platelet transfusion and follow-up.

Abciximab is a chimeric (murine/human) monoclonal antibody fragment (c7E3 Fab) specific for an epitope on the platelet GPIIb/IIIa complex close to a critical binding site for fibrinogen, inhibiting its reaction with the activated GPIIb/IIIa integrin (alpha IIb/beta 3) and inhibiting platelet–platelet integration and thrombus formation.^{2,16–18} Abciximab causes a dose-dependent

inhibition of platelet function, with maximal antiplatelet effect within minutes of infusion, returning to baseline 12–48 hours after cessation, due to rapid platelet turnover.^{11,12,19–22} It has a short plasma half-life of 10–30 min, and a long biological half-life due to its strong receptor affinity and irreversible platelet binding.^{1,23} This profile allows for the reversibility of significant bleeding time with platelet transfusion, which reduces the drug's receptor occupancy on platelet surfaces to $<50\%$, the critical threshold associated with bleeding time prolongation.^{1,24}

Diagnosis of acute profound abciximab-induced thrombocytopenia requires considering a differential including pseudothrombocytopenia and HIT.^{25,26} Pseudothrombocytopenia, as opposed to true thrombocytopenia, involves neither increased thrombotic or haemorrhagic risk nor clinical significance as it is caused by ethylenediaminetetraacetic acid-dependent in vitro platelet clumping, which can be detected on peripheral smear or repeat platelet count with citrate anticoagulated blood.^{7,27} HIT differs from abciximab-induced thrombocytopenia in that it typically develops over several days as opposed to the rapid onset of abciximab-induced thrombocytopenia, with Type 1 HIT developing over 2–4 days and Type 2 HIT (the most clinically significant form of HIT) 5–8 days following the initial heparin exposure.^{23,28,29} Other medications commonly causing profound thrombocytopenia should also be considered (ie, sulfonamides, thiazides, quinine, quinidine and phenytoin).²³ Outpatient presentation of acute thrombocytopenia is commonly due to pseudothrombocytopenia, drug-induced, idiopathic thrombocytopenic purpura, or gestational and less commonly due to chronic liver disease, myelodysplastic syndrome, congenital syndromes or HIV.³⁰

Close monitoring of platelet count is critical to early evaluation and treatment of abciximab-induced thrombocytopenia as rapid identification is essential to preventing major haemorrhage, and although some patients may exhibit petechial haemorrhages, bleeding from catheterisation sites, gastrointestinal haemorrhage or haematoma, other patients may be entirely asymptomatic.^{1,6,24,31} Because of the risk of abciximab-induced thrombocytopenia, the platelet count should routinely be performed prior to abciximab treatment as well as 2–4 hours later to permit early diagnosis and treatment.^{7,11,15,28} Management is dependent on thrombocytopenia severity, comorbidity and complications with the most effective management including immediate cessation of treatment, platelet transfusion and monitoring the platelet count at least daily until resolution.^{3,6,7,30}

Learning points

- ▶ Close monitoring of platelet count is critical to early evaluation and treatment of abciximab-induced thrombocytopenia as rapid identification is essential to preventing major haemorrhage.
- ▶ Management includes immediate cessation of treatment, platelet transfusion, and platelet count monitoring.
- ▶ Differential diagnosis includes heparin-induced thrombocytopenia and pseudothrombocytopenia.
- ▶ The risk factors for abciximab-induced thrombocytopenia include age >65 years, weight <80 kg and a baseline platelet count $<200\,000/\text{L}$.

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