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Acute Severe Thrombocytopenia Occurring After Administration of Eptifibatide Postpones Emergent Coronary Artery Surgery

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Abstract

Introduction: Eptifibatide is a platelet glycoprotein IIb/IIIa (GP IIb/IIIa) receptor antagonist that inhibits fibrinogen binding to the activated GP IIb/IIIa site and prevents platelet-platelet interaction and clot formation. GP IIb/IIIa inhibitors improve outcome in patients undergoing percutaneous coronary intervention for acute coronary syndrome. Thrombocytopenia is a complication of GP IIb/IIIa inhibitors, but severe thrombocytopenia is unusual. Most reported cases of severe thrombocytopenia after eptifibatide occurred in patients with acute coronary syndrome. The authors describe a patient who developed acute profound thrombocytopenia after receiving eptifibatide before emergent coronary artery bypass graft surgery.

Case Presentation: A 67-year-old man with a normal platelet count (220 K/uL) developed atrial fibrillation, left bundle branch block, and respiratory insufficiency consistent with acute coronary syndrome two days after colectomy. He received eptifibatide during cardiac catheterization, where three-vessel coronary artery disease was encountered. Emergent coronary artery surgery was planned, but the platelet count before surgery was 2 K/uL. Eptifibatide was discontinued, surgery was postponed, and acute coronary syndrome was treated with intraaortic balloon counterpulsation.

Conclusions: The authors describe the second reported case of eptifibatide-induced severe thrombocytopenia associated with cardiac surgery. In this case, discontinuation of eptifibatide and transfusion of apheresis platelets increased the platelet count (137 K/uL) the following day, and the patient subsequently underwent successful coronary artery surgery using cardiopulmonary bypass.

Keywords: Eptifibatide, Acute Thrombocytopenia, GP IIb/IIIa Inhibitor, Coronary Artery Disease, Acute Coronary Syndrome, Cardiac Surgery, Coronary Artery Bypass

1. Introduction

Eptifibatide is a platelet glycoprotein IIb/IIIa (GP IIb/IIIa) receptor antagonist that inhibits fibrinogen binding to the activated GP IIb/IIIa site (1). GP IIb/IIIa receptor blockade by eptifibatide prevents platelet-platelet interaction and clot formation. GP IIb/IIIa inhibitors (e.g., eptifibatide, abciximab) improve outcome in patients undergoing percutaneous coronary intervention for acute coronary syndrome (2, 3). Thrombocytopenia is a complication of GP IIb/IIIa inhibitors, but severe thrombocytopenia (< 20 K/uL) is unusual (0.2% to 1%) (2, 4, 5). Most reported cases of severe thrombocytopenia after eptifibatide occurred in patients with acute coronary syndrome. The authors describe a patient who developed acute profound thrombocytopenia after receiving eptifibatide before emergent coronary artery bypass graft (CABG) surgery.

2. Case Presentation

A 67-year-old man with known coronary artery disease and a history of stent implantation underwent a total colectomy for ulcerative colitis. His perioperative course was unremarkable. He was transferred to the ward after surgery where he initially made an uneventful recovery. On the second postoperative day, the patient developed new atrial fibrillation with a rapid ventricular response, dyspnea at rest, hypoxemia, and diaphoresis. The patient was transferred to the intensive care, where he was intubated and mechanically ventilated for acute respiratory insufficiency. A computed tomography scan was performed that excluded pulmonary embolism. An electrocardiogram indicated the presence of new left bundle branch block. Coronary angiograms demonstrated severe stenoses of the left anterior descending and the left circumflex coronary arteries, and proximal occlusion of right coronary artery, which filled in a retrograde manner from the left-sided vessels. The cardiologists attempted but were unable to implant a stent in the severely nar-

rowed left circumflex coronary artery. The patient received two doses of eptifibatide (9 mg each) during the procedure and an intravenous infusion of the drug was begun (2 mcg/kg/min). A heparin infusion was also initiated, but the patient did not receive clopidogrel. An intraaortic balloon pump (IABP) was placed to improve coronary perfusion, cardiothoracic surgery and anesthesia were consulted, and emergent CABG was planned.

Shortly before the patient was transported to the operating room, the laboratory reported that platelet count had acutely fallen to 2 K/uL from the value of 220 K/uL that was measured before administration of eptifibatide. The severe thrombocytopenia was confirmed with peripheral blood smear. A second blood sample obtained in citrate verified the thrombocytopenia and excluded pseudothrombocytopenia. The infusions of eptifibatide and heparin were immediately discontinued, CABG surgery was postponed, and the patient was treated medically overnight in the intensive care unit while being monitored closely for bleeding. Laboratory tests to determine platelet activity (e.g., thromboelastography, platelet function assays) were not performed because the profound thrombocytopenia was a direct contraindication to surgery. Two units of single donor apheresis platelets were transfused. The platelet count increased appropriately with this transfusion (approximately 50 K/unit) and eventually rose to 137 K/uL the following morning. The patient remained stable with IABP support and was subsequently taken to the operating room for CABG, which proceeded uneventfully using cardiopulmonary bypass. Reverse saphenous vein grafts were used to bypass the second obtuse marginal and posterior descending coronary arteries. The left internal mammary artery was used to bypass the left anterior descending coronary artery. The IABP and intravenous inotropic medications were used to separate from cardiopulmonary bypass. The patient received additional autologous blood products including platelets to obtain hemostasis. The patient's postoperative course was complicated by acute kidney injury treated with continuous veno-venous hemodialysis and a sternal infection that required surgical debridement and long-term antibiotic therapy. The patient was eventually discharged to an inpatient rehabilitation facility.

3. Discussion

To the authors' knowledge, only one previous case of eptifibatide-induced severe thrombocytopenia associated with cardiac surgery has been reported (6). In this case, severe thrombocytopenia was observed six hours after infusions of eptifibatide and heparin were begun in a man with an acute myocardial infarction. This patient underwent emergent CABG after platelet transfusion partially restored the platelet count because his cardiovascular status continued to deteriorate (6). In contrast, the authors opted to postpone surgery in the current patient because he remained hemodynamically stable with IABP support and his acute respiratory insufficiency was appropriately managed using mechanical ventilation. Discontinuation of the eptifibatide infusion and platelet transfusion increased the patient's platelet count to a level (137 K/uL) that was safe for cardiac surgery the following morning.

GP IIb/IIIa inhibitor-induced thrombocytopenia is usually observed after a second exposure to the drug because of antibody formation resulting from initial treatment (7). This mechanism accounts for the relatively common occurrence of profound thrombocytopenia (approximately 10%) observed after a second dose of abciximab (7). In contrast, eptifibatide-induced thrombocytopenia usually occurs with the initial exposure because of preexisting antibodies directed against the ligand-occupied receptor site. While it is possible to identify these antibodies before exposure to the GP IIb/IIIa inhibitor, routine testing is usually not performed before eptifibatide is administered (1). Other causes of thrombocytopenia need to be excluded before the diagnosis of eptifibatide-induced thrombocytopenia can be established. Pseudothrombocytopenia may be observed using automated complete blood cell analysis when blood samples are collected in EDTA-containing tubes, but absence of platelet clumping in a peripheral blood smear confirms the diagnosis of thrombocytopenia (8). Heparin-induced thrombocytopenia (HIT) was also considered because the patient received subcutaneous heparin for deep vein thrombosis prophylaxis after the colectomy. However, the precipitous drop in platelet count and its temporal relationship to administration of eptifibatide concomitant with a negative platelet factor-4 assay made HIT highly unlikely. The magnitude of thrombocytopenia observed in HIT is also rarely as profound as that observed after administration of eptifibatide. Indeed, heparin was also used successfully for cardiopulmonary bypass anticoagulation during the patient's CABG surgery without further the development of further thrombocytopenia. Thrombocytopenia may be observed after administration of clopidogrel (7), but this type of thrombocytopenia most often presents days to weeks after drug exposure and the patient did not receive this medication. Isolated thrombocytopenia and thrombotic thrombocytopenia were also excluded on the basis of the patient's history. As was done in the current patient, a platelet count is strongly recommended within two to six hours after eptifibatide is administered to detect developing thrombocytopenia and intervene to prevent complications (9).

Footnote

Authors' Contribution: Brent T. Boettcher: cared for the patient in the operating room and wrote drafts of the manuscript; the author has read the final draft of the manuscript and approves it for submission; Timothy J. Olund: cared for the patient in the operating room and wrote drafts of the manuscript; the author has read the final draft of the manuscript and approves it for submission; Paul S. Pagel: wrote and edited drafts of the manuscript; the author has read the final draft of the manuscript and approves it for submission.

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