Abciximab-induced alveolar hemorrhage after percutaneous coronary intervention

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Abciximab, a platelet glycoprotein (GP) IIb/IIIa inhibitor, has been shown to improve clinical outcomes in patients undergoing percutaneous coronary intervention. However, there is a well-documented increase in bleeding risk associated with the use of this agent. Spontaneous pulmonary hemorrhage is a particularly rare and easily misdiagnosed complication that requires early diagnosis to ensure patient survival. A 61-year-old man presented to the emergency department with chest pain and inferolateral ST elevation on electrocardiogram. A paclitaxel drug-eluting stent was then placed in the left circumflex artery, without complications. Abciximab (a bolus of 0.25 mg/kg followed by an infusion of 10 mg/min for 12 h) was given. Approximately 20 min later, the patient developed dyspnea and hemoptysis. A chest radiograph revealed new bilateral diffuse interstitial infiltrates, and the patient was started on empirical antibiotics for pneumonia. Because of increasing dyspnea and somnolence, the patient was intubated and bronchoscopy was performed, revealing serial hemorrhagic returns from the left lower lobe, diagnostic of diffuse alveolar hemorrhage and judged to be secondary to abciximab, given the time course. All antiplatelet and antithrombotic agents were stopped. The patient stabilized over the next several days, with some recurrent hemoptysis, and was successfully extubated seven days later. Prognosis remains poor in GP IIb/IIIa inhibitor-induced pulmonary hemorrhage, and early diagnosis is critical so that antithrombotic and antiplatelet agents may be discontinued in a timely manner. A high degree of suspicion is required when treating a patient who presents with dyspnea and new radiological infiltrates after receiving a GP IIb/IIIa inhibitor.

Key Words: *Abciximab; Diffuse alveolar hemorrhage; Glycoprotein IIb/IIIa inhibitors*

Hémorragie alvéolaire secondaire à l'administration d'abciximab après une intervention coronarienne percutanée

L'abciximab, un inhibiteur de la glycoprotéine (GP) plaquettaire IIb/IIIa, améliore l'état clinique des patients soumis à une intervention coronarienne percutanée. Cependant, l'utilisation du médicament comporte un risque accru, et bien documenté, d'hémorragie. L'hémorragie pulmonaire spontanée est une complication particulièrement rare et souvent mal diagnostiquée, qui exige pourtant un diagnostic précoce pour assurer la survie du patient. Voici le cas d'un homme de 61 ans qui s'est présenté au service d'urgence pour des douleurs thoraciques et qui présentait un sus-décalage inféro-latéral du segment ST à l'électrocardiographie. On lui a donc posé une endoprothèse à élution de paclitaxel dans l'artère auriculo-ventriculaire, sans complications; on lui a également administré de l'abciximab (bolus de 0,25 mg/kg, suivi d'une perfusion de 10 mg/min, pendant 12 h). Une vingtaine de minutes plus tard, le patient a commencé à présenter de la dyspnée et de l'hémoptysie. Une radiographie pulmonaire a révélé la présence de nouveaux infiltrats interstitiels diffus, bilatéraux, et un traitement antibiotique empirique a été instauré pour soigner une pneumonie. Comme le patient devenait de plus en plus dyspnéique et somnolent, il a fallu l'intuber; une bronchoscopie a été pratiquée, et elle a ramené du lobe inférieur gauche des prélèvements hémorragiques, en série, qui ont signé le diagnostic d'hémorragie alvéolaire diffuse, jugée secondaire à l'administration d'abciximab, compte tenu du temps écoulé. L'administration des antiplaquettaires et des antithrombotiques a donc été interrompue. L'état du patient s'est stabilisé au cours des jours suivants, bien qu'il se soit produit d'autres hémoptysies, et l'extubation a été réalisée avec succès sept jours plus tard. Le pronostic d'hémorragie pulmonaire provoquée par un inhibiteur de la GP IIb/IIIa est sombre, et il est extrêmement important de reconnaître l'affection le plus tôt possible de manière à interrompre l'administration des antithrombotiques et des antiplaquettaires en temps opportun. Un diagnostic d'hémorragie doit être fortement envisagé chez le patient qui consulte pour de la dyspnée et qui présente de nouveaux infiltrats à la radiographie après l'administration d'un inhibiteur de la GP IIb/IIIa.

Abciximab, a platelet glycoprotein (GP) IIb/IIIa inhibitor, has been shown to improve clinical outcomes in patients undergoing percutaneous coronary intervention (PCI). However, there is a well-documented increase in bleeding risk associated with use of this agent. Several types of bleeding, including groin site, intracranial, gastrointestinal, genitourinary and pulmonary, have been described. Spontaneous pulmonary hemorrhage is a particularly rare and easily misdiagnosed complication that requires early diagnosis to ensure patient survival.

CASE PRESENTATION

A 61-year-old man with no previous history of coronary artery disease presented to the emergency department for evaluation of chest pain associated with diaphoresis. His initial electrocardiogram

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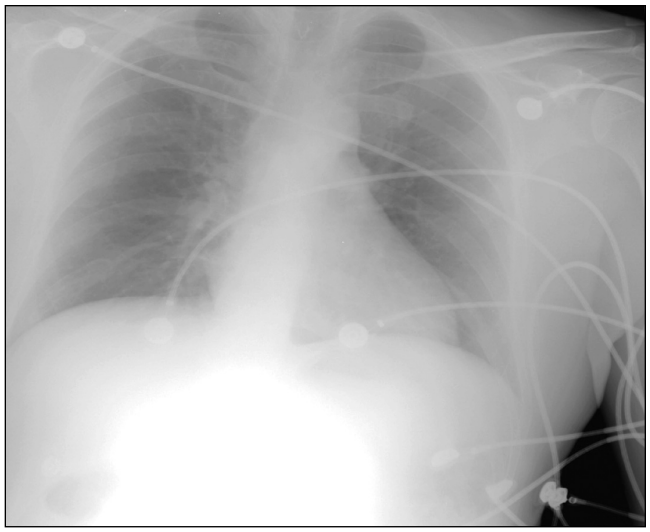

Figure 1) *Normal chest film on admission*

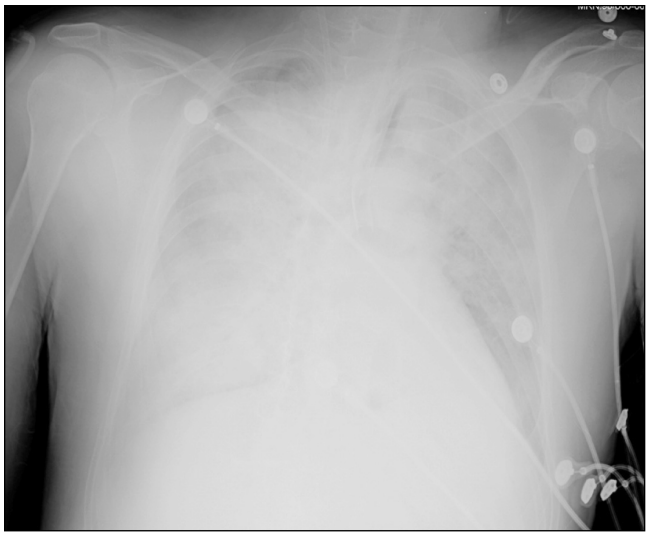

Figure 2) *Chest film 12 h after first abciximab administration, revealing bilateral interstitial infiltrates*

showed inferolateral ST elevation, and therapy for acute myocardial infarction was initiated. The patient was given acetylsalicylic acid (325 mg) and unfractionated heparin (a 5000 U bolus followed by a 1100 U/h infusion), and cardiology consultation was requested.

Portable chest radiograph results were unremarkable (Figure 1). The initial laboratory evaluation revealed normal cardiac enzyme levels, complete blood count and coagulation profile.

Coronary angiography revealed thrombotic occlusion of the mid-left circumflex artery and a long area of 80% to 90% mid-vessel stenosis of a small, codominant right coronary artery. Percutaneous revascularization of the left circumflex artery was performed using balloon angioplasty, followed by placement of a paclitaxel-eluting stent (Taxus; Boston Scientific, USA), resulting in restoration of Thrombolysis In Myocardial Infarction (TIMI) grade 3 flow. Abciximab was started at the time of intervention (a 0.25 mg/kg bolus followed by a 10 mg/min infusion for 12 h). The activated clotting time was 272 s before the abciximab bolus. There were no complications during this intervention.

Approximately 20 min after the abciximab bolus was given, the patient became acutely dyspneic and hypoxic, and developed a cough that produced pink, frothy sputum. Auscultation of his lungs revealed new bilateral rhonchi, but his cardiac examination remained normal. Intravenous furosemide (40 mg) and morphine (4 mg) were administered for presumed pulmonary edema, and supplemental oxygen was provided via a face mask. After approximately 30 min, the patient's dyspnea resolved, and his oxygen saturation remained stable on supplemental oxygen.

In the cardiac intensive care unit, the patient was continued on an abciximab infusion and received a loading dose of clopidogrel (300 mg). He remained hemodynamically stable but developed paroxysms of coughing that produced progressively bloody sputum. Approximately 12 h post-PCI, the patient became febrile and hypotensive, and experienced frank hemoptysis. The abciximab infusion was stopped, and a pulmonary artery catheter was placed, revealing a central venous pressure of 3 mmHg, a pulmonary artery systolic pressure of 30 mmHg and a pulmonary capillary wedge pressure of 13 mmHg. The patient's systemic blood pressure was 80/60 mmHg, with heart rate of 107 beats/min. Hemodynamic support was provided with intravenous fluids and a neosynephrine drip.

Over the next 18 h, the patient's respiratory status deteriorated, and a chest radiograph revealed bilateral diffuse interstitial infiltrates, initially thought to be pulmonary edema or pneumonia (Figure 2). A bedside echocardiogram was normal. The patient was started on empirical therapy for pneumonia with levofloxacin and clindamycin.

The patient underwent bronchoscopically guided intubation for progressive acute respiratory distress syndrome physiology. Because focal hemorrhage consequent to anticoagulation was a concern, a double-lumen endotracheal tube was used to isolate each lung and to prevent potential contralateral aspiration of blood from the more involved lung. The patient was diagnosed with diffuse alveolar hemorrhage, given the progressive hemorrhagic returns on serial bronchoalveolar lavage and the appearance of more than 20% hemosiderin-laden alveolar macrophages on lavage specimen.

His hemoglobin dropped to 88 g/L (8.8 g/dL), but all other laboratory values, including his platelet count and coagulation panel, remained normal. Acetylsalicylic acid and clopidogrel were stopped, and he underwent a transfusion of two units of packed red blood cells.

The patient's hemodynamic and respiratory status stabilized over the next five days, with only a minor recurrence of hemoptysis. He was successfully extubated on hospital day 7 and discharged in good condition on day 9.

DISCUSSION

Pulmonary hemorrhage associated with platelet GP IIb/IIIa inhibitors is a serious and rare complication, and has previously been described in various case reports (1-5). It has been reported to be associated with all three GP IIb/IIIa inhibitors approved for use in PCI, including abciximab, eptifibatide and tirofiban, with respective incidences of 0.7%, 0.5% and 0.9%, and an overall incidence of 0.68% (seven of 1020 patients reviewed) (1).

Diffuse alveolar hemorrhage secondary to GP IIb/IIIa inhibitors can be very difficult to diagnose. Dyspnea after PCI has a wide differential diagnosis, and may initially be diagnosed as pulmonary thromboembolism, pulmonary edema, aspiration pneumonitis or pneumonia, as in this patient. If one maintains a high degree of suspicion for this complication, the offending agents, potentially including all antiplatelet and antithrombotic agents, may be discontinued in a timely manner.

Treatment for pulmonary hemorrhage is supportive. All antiplatelet and antithrombotic medications, including thienopyridines, should be discontinued once pulmonary hemorrhage is suspected. Early bronchoscopy in severe cases is critical for localization and diagnosis. The majority of reported cases have required blood transfusion. Platelet transfusion may be considered in patients who

have received abciximab, but may not be effective in reversing the effects of tirofiban or eptifibitide. In this case report, activated factor VII and platelet transfusions were considered to reverse or attenuate the effects of the abciximab, but the risk of in-stent thrombosis was judged to be too high.

The prognosis remains poor in patients with GP IIb/IIIa inhibitor-induced pulmonary hemorrhage, and mortality is high. In previously reported case series (3-5), mortality ranged from 29% to 50%. As illustrated in the present case, pulmonary hemorrhage may often initially be misdiagnosed as pulmonary edema or pneumonia. A high degree of suspicion is required when treating a patient who presents with dyspnea, hemoptysis, a drop in hemoglobin or with new radiological infiltrates after receiving a GP IIb/IIIa inhibitor as part of the management of acute coronary syndrome and PCI.

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