

Alveolarna krvavitev kot zaplet po kombiniranem zdravljenju z antiagregacijskimi in antikoagulantnimi zdravili pri primarni koronarni intervenciji pri bolniku z akutnim koronarnim sindromom z elevacijo ST veznice – prikaz primera

Alveolar hemorrhage after treatment with combined antiplatelet and anticoagulation therapy before and during primary coronary intervention in acute coronary syndrome with ST elevation – a case report

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Izvleček

Z antiagregacijskim in antikoagulantnim zdravljenjem začnemo pri bolnikih z akutnim koronarnim sindromom (AKS) z elevacijo ST veznice že pred primarno koronarno intervencijo (PCI). Eptifibatid je zaviralec glikoproteinskih receptorjev IIB/IIIa na membrani trombocitov in ga pogosto uporabljamo skupaj s standardnim heparinom za preprečevanje tromboz po PCI. Krvavitve so zaplet po PCI in se najpogosteje pojavijo na vbodnem mestu in so pogostejše pri starejših bolnikih. Alveolarna krvavitev je redek zaplet po kombiniranem zdravljenju z antiagregacijskimi in antikoagulantnimi zdravili. Opisano bo primer 43-letnega kadilca, ki se je zdravil zaradi miokardnega infarkta z dvigom veznice ST. Pred primarno PCI je prejel standardni heparin in dvojno antiagregacijsko terapijo. Kakšnih 5 minut po intrakoronarni aplikaciji eptifibatida so se pojavile hemoptize. Potrebna je bila

Abstract

Platelet inhibition with aspirin and systemic anticoagulation with unfractionated heparin to reduce the incidence of recurrent thrombosis after primary coronary intervention (PCI) has been the standard of care for patients with acute coronary syndrome (ACS) with ST elevation for some time. Eptifibatide is the platelet membrane glycoprotein IIB/IIIa inhibitor that is often used. Bleeding complications occur most often at sites of vascular access and are more common in elderly patients. Alveolar hemorrhage with hemoptysis is a rare complication. We describe the case of a 43-year old smoker with an ST elevation myocardial infarction admitted for PCI. He was treated with standard anticoagulation and dual antiplatelet therapy before admission. Hemoptysis began approximately five minutes after the intracoronary application of eptifibatide at the end of the procedure. Supportive

intubacija, mehanična ventilacija, transfuzija koncentriranih eritrocitov in ukinitve vseh antikoagulantnih sredstev. Alveolarna krvavitev je življenje ogrožujoč zaplet po PCI in zahteva intenzivno in hitro zdravljenje.

care including endotracheal intubation, mechanical ventilation, transfusion of packed red blood cells and reversal of all anticoagulation. Alveolar hemorrhage is life-threatening but adequate intensive supportive measures can be life-saving.

INTRODUCTION

Platelet inhibition with aspirin and systemic anticoagulation with unfractionated heparin (UFH) to reduce the incidence of recurrent thrombosis after primary coronary intervention (PCI) has been the standard of care for patients with acute coronary syndrome (ACS) with ST elevation for some time. Eptifibatide is a cyclic heptapeptide inhibitor of the platelet membrane GP IIb/IIIa receptor and reduces the incidence of recurrent thrombosis when administered at the time of PCI (2). However, it increases the risk of bleeding complications, particularly at vascular puncture sites but also in intracranial, gastrointestinal and retroperitoneal sites (3,4,5). Very rarely, pulmonary alveolar hemorrhage (AH) can occur. We present a patient with pulmonary AH after the use of combined anticoagulant and antiplatelet therapy with eptifibatide, UHF, clopidogrel and aspirin.

Case report

A 43-year old smoker was admitted to our University Clinic from a regional hospital with symptoms and signs of anterior ST elevation myocardial infarction. On admission, the platelet count and coagulation profile were within normal limits and he was normotensive and in Killip class I heart failure. Before admission he received oral clopidogrel (600 mg), aspirin (500 mg), sublingual ni-

trate and standard heparin (5000 IE) i.v. After 45 minutes of transport to our cardiac catheterization laboratory, primary PCI was performed. Coronary angiography revealed an obstruction in the proximal part of the left anterior descending (LAD) coronary artery. He had immediate balloon angioplasty with bare metal stent implantation, resulting in TIMI 3 flow. During the procedure intracoronary boluses of eptifibatide (2 µg/kg/minute) were administered twice, after which he became hypotensive (blood pressure 80/60 mmHg) and treatment with adrenalin and dopamine (up to 8 µg/kg/minute) was needed to achieve normotension. Approximately five minutes after the second intracoronary bolus of eptifibatide [edit okay?] the patient started to cough uncontrollably and massive hemoptysis followed. He was admitted to the intensive care unit (ICU) with a blood pressure of 120/55 mm Hg and heart rate of 70/minute. Continuous electrocardiographic and SaO₂ monitoring was commenced and central venous and arterial catheters were inserted to measure arterial and central venous pressure invasively. The patient was dyspneic, pale, and hypoxic with SaO₂ 91% on 100% oxygen (pO₂ /FiO₂ 112). Endotracheal intubation and mechanical ventilation were required due to severe respiratory failure. Emergency bronchoscopy revealed diffuse pulmonary AH. During the procedure, several blood clots were removed and the patient received 1700 mL of packed red blood cells and 625 mL of fresh fro-

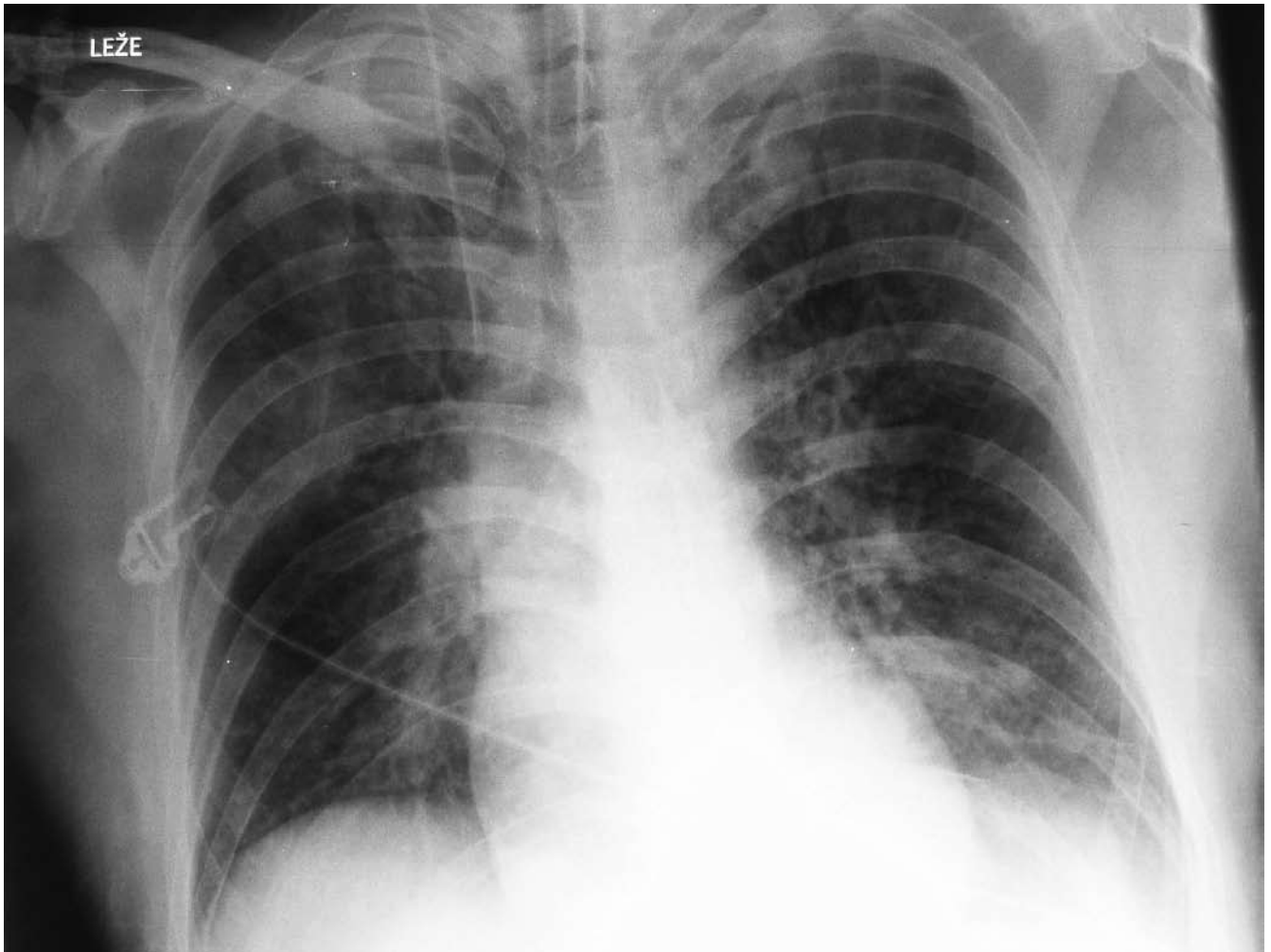


Figure 1. Pulmonary alveolar infiltrates on the chest radiograph in our 43 year old smoker with ST – segment elevation myocardial infarction. Those infiltrates represent alveolar hemorrhage after the combined treatment with clopidogrel Aspirin, Heparin and eptifibatide.

zen plasma within the first hour. Antiplatelet and anticoagulation therapy was discontinued and he was treated with protamine sulphate (25 mg i.v.). Within the next few hours iv. dopamine was replaced by noradrenaline (up to 10 $\mu\text{g}/\text{kg}/\text{min}$) to maintain normal blood pressure. The signs and symptoms of abundant AH ceased after 12 hours of treatment. To prevent in-stent thrombosis, clopidogrel was administered on the second day and aspirin was added 5 days after admission to ICU. On the 13th day the patient was transferred back to the regional hospital

DISCUSSION

Major and minor bleeding events may complicate the periprocedural course of patients who undergo primary PCI for ST elevation MI and receive combined antiplatelet and anticoagulation therapy, including a GP IIb/IIIa inhibitor. The signs and symptoms of pulmonary AH are nonspecific. Hemoptysis and/or hemoptoe (spitting blood), together with pulmonary infiltrates on chest radiograph (ure 1) and arterial hypoxia, can be the consequences of a broad spectrum of clinical conditions such as pulmonary infection, pulmonary edema, aspiration pneu-

monia, endobronchial malignancy and pulmonary thromboembolism. Alternatively, bloody expectoration can also mimic acute upper gastrointestinal bleeding, which can be excluded only with oesophagogastroduodenoscopy. In our case the final identification of the bleeding site was possible only after the patient was intubated and bronchoscopy was performed, with the subsequent removal of massive blood clots.

The severe respiratory compromise with a pO_2/FiO_2 112 was due to the combined effect of AH and concomitant heart failure due to cardiogenic pulmonary edema. As in almost all reported cases of AH after combined antiplatelet and anticoagulation treatment, we observed normal platelet counts on admission and after the PCI (3,4,5).

Iskander et al in their retrospective analysis reviewed the incidence and risk factors of AH in the setting of either eptifibatide or abciximab therapy and observed that for patients treated with GP IIb/IIIa inhibitors the risk for AH was significantly increased in comparison to the control group, and that this was particularly noticeable for eptifibatide (6).

However, additional individual risks factors for AH

after intense antiplatelet and anticoagulation therapy are not completely understood. In almost all reported cases the patients were smokers or ex smokers or had chronic obstructive pulmonary disease. Another important risk for AH was pulmonary edema with increased pulmonary wedge pressure. Concordant with this, our patient was an active smoker and had cardiogenic shock with pulmonary edema during the primary PCI.

We cannot be certain whether eptifibatide was responsible for the AH in this case or whether it resulted from the cumulative effect of the antiplatelet and anticoagulation therapy. However, AH began immediately after the intracoronary bolus of eptifibatide, so we can assume that it was the proximate cause.

Our conclusions are that AH is a rare but potentially fatal complication after primary PCI for ST elevation myocardial infarction when combined antiplatelet and antithrombotic therapy are administered. Emergent support of respiratory function with intubation and mechanical ventilation in addition to temporary cessation of antiplatelet and anticoagulation therapy saves lives.

REFERENCES

1. Silber S, Albertsson P, Aviles FF, Camici PG, Colombo A, Hamm C et al. Guidelines for percutaneous intervention. The task force for percutaneous coronary interventions of the European Society of Cardiology. *Eur Heart J* 2005; 26:804–47
2. Popma JJ, Ohman EM, Weitz J, Lincoff AM, Harrington RA, Berger P. Antithrombotic therapy in patients undergoing percutaneous coronary intervention. *Chest* 2001; 119 Suppl: 321S–61S
3. The EPIC Investigators. Use of a monoclonal antibody directed against the platelet glycoprotein IIb/IIIa receptor in high-risk coronary angioplasty. *N Engl J Med* 1994; 330: 956–61
4. The EPILOG Investigators. Platelet glycoprotein IIb/IIIa receptor blockade and low-dose heparin during percutaneous coronary revascularization. *N Engl J Med* 1997; 336:1689–96
5. The CAPTURE Study. Randomized placebo-controlled trial of abciximab before and during coronary intervention in refractory unstable angina. *Lancet* 1997; 349:1429–35
6. Iskander SB, Kasasbeh ES, Mechleb BK, Garcia I, Jackson A, Fahrig Set al. Alveolar hemorrhage: an underdiagnosed complication of treatment with glycoprotein IIb/IIIa inhibitors. *J Interv Cardiol* 2006; 19: 356–63