Eptifibatide induced acute thrombocytopenia. Case report of 80- years old man with acute coronary syndrome

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ABSTRACT

Introduction: Glycoprotein (Gp) IIb/IIIa is a platelet receptor participating in platelet aggregation. According to ESC guidelines, glycoprotein IIb/IIIa inhibitors might be considered during percutaneous coronary interventions in patients with the acute coronary syndrome.

Purpose: A case study of profound thrombocytopenia in 80-year-old man with the acute coronary syndrome.

Case presentation: An 80-year-old, medication-naive man with acute coronary syndrome was admitted to the Department of Invasive Cardiology. Due to the unsuccessful invasive strategy, an intracoronary bolus of Gp IIb/IIIa inhibitor – eptifibatide - was administered. During the following intravenous infusion, large subcutaneous hematomas were observed. Eptifibatide infusion was discontinued. Drop in platelet count to 1 thou/μL without significant anemia was registered. A control sample in sodium citrate showed similarly low platelet count - 2 thou/uL. Acetylsalicylic acid and clopidogrel were discontinued, steroids were introduced. Neither PLT nor FFP transfusion were necessary. Consecutive lab tests showed the gradual increase of PLT up to 35 thou/μL at discharge. A week later, the patient did not complain of any cardiovascular or bleeding symptoms; hematomas resented significant involution. Laboratory findings were normal. During follow-up visit 30 days after the discharge, the patient presented no cardio-vascular symptoms.

Conclusions: There are patients at risk of drug-induced thrombocytopenia, especially those with impaired kidney function and the elderly. In such cases, decisions concerning anti-platelet and anti-thrombotic therapy should be taken cautiously. Because of its rare occurrence, every case of severe thrombocytopenia in ACS patients should be reported. Moreover, such patients should be followed-up to minimalize risk of similar adverse events in the future.

Keywords: Thrombocytopenia, glycoprotein IIb/ IIIa inhibitors, acute coronary syndrome

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INTRODUCTION

Glycoprotein (Gp) IIb/IIIa is a platelet receptor participating in platelet aggregation. The receptor undergoes activation after fibrinogen or vWF binding. In everyday practice, there are three intravenous Gp IIb/IIIa inhibitors – abciximab, eptifibatide, and tirofiban. According to current ESC guidelines concerning the management of Acute Coronary Syndromes in patients presenting without persistent ST-segment elevation glycoprotein, IIb/IIIa inhibitors should be considered in bailout situations or thrombotic complications during percutaneous coronary interventions [1].

Purpose

A case study of profound thrombocytopenia in 80-year-old man with an acute coronary syndrome.

CASE REPORT

An 80-year-old man, with no history of cardiovascular diseases, medication-naive, with acute coronary syndrome was transferred to the Department of Invasive Cardiology from the Regional Hospital for coronarography. He had a history of recurrent chest pain on exertion within the last few days. On the admission day, he had an hour lasting chest pain at rest which forced him to visit ER.

ECG revealed no signs of ischaemia, laboratory findings presented with the elevated and increasing troponin concentrations, increased creatinine with decreased eGFR (30 - 45 ml/(min · 1,73 m²) i.e. G3b chronic kidney disease stage according to KDIGO.

Patient was given loading dose of ASA and clopidogrel in the Regional Hospital. On admission to the Department of Invasive Cardiology patient presented with chest pain, BP 160/110mmHg, ECG presented sinus tachycardia 105/min., normal axis, first-degree AV block, deeply inverted T waves in the anterior precordial leads (Wellens syndrome). He was scheduled for immediate coronarography which revealed subtotal occlusion of LAD in the mid-segment, with no significant narrowing's in the other coronary arteries.

After predilatation the slow-flow phenomenon was observed, which resulted in severe bradycardia and hypotension. Due to the unsuccessful invasive strategy the intracoronary bolus of Gp IIb/IIIa inhibitor – eptifibatide was administered.

The treatment resulted in the improvement of patient's condition which enabled the continuation of revascularization and drug eluting stent implantation. Intravenous bolus of eptifibatide was administered directly after the procedure followed by intravenous infusion.

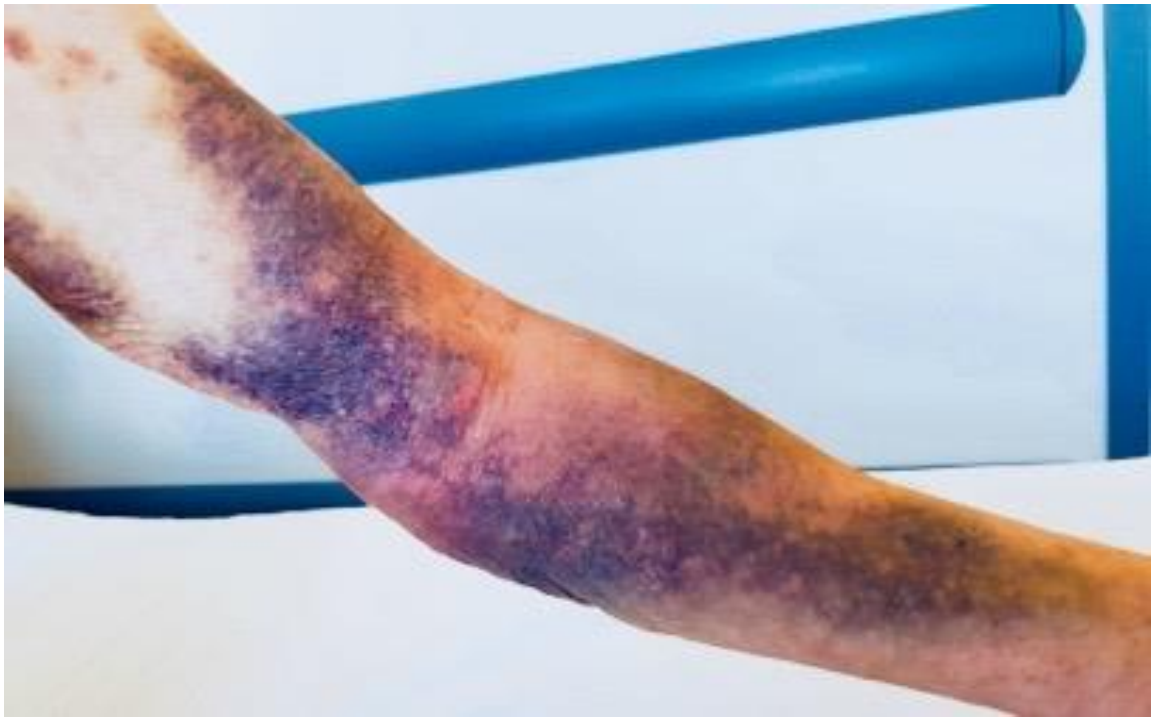
During the post-procedural observation patient was hemodynamically stable, complained with chest discomfort, the ECG presented sinus tachycardia and negative T waves in the anterior precordial leads.

Echocardiography showed the heart of normal size with no significant valvular disease, mild systolic dysfunction of the left ventricle (EF=43%) with akinesis of the apical segments of the anterior and inferior wall and ventricular septum. Laboratory findings showed increased necrotic markers and creatinine concentrations – 2.32 mg/dL, PLT 276 thou/µL, with no other abnormalities.

Eptifibatide infusion was continued according to the schedule. During the infusion patient complained with enlarging subcutaneous hematomas of the forearms – within the vascular access sites – right radial artery and brachial vein [Phot. 1].

Eptifibatide infusion was discontinued. Lab test collected after 12 hours presented drop in platelet count amounting to 1 thou/µL, RBC accounting for 3.82 mln/µL, HGB concentration – 11.5 g/dL. Repeat testing on a sample collected in sodium citrate showed similarly low platelet count - 2 thou/uL, therefore acetylosalicylic acid and clopidogrel were discontinued, and steroids were introduced to the therapy - hydrocortisone 100mg t.i.d. Neither PLT nor FFP transfusion was considered necessary. Consecutive lab tests, collected in the 36th hour of the follow-up revealed the increase of PLT- 15 thou/µL, followed with 35 thou/µL. Patient remained asymptomatic, did not present with any chest discomfort, no active bleeding was observed, the forearm hematomas did not enlarge. On day 3 acetylsalicylic acid was brought back in treatment, followed with the reintroduction of clopidogrel on the next day after PLT reached the count of 45 thou/µL. Forearm hematomas were treated locally with heparin gel, the patient remained hemodynamically stable, did not complain of any chest pain. HGB concentration remained stable in the following tests, follow-up lab findings on day 6 were as follows: WBC 8.89 thou/µL, RBC 3.73 mln/µL, HGB 11.3 g/dL, PLT 124 thou/µL, creatine 1.78 mg/dL, eGFR 39 ml/min [Fig. 1].

Patient was discharged home on day 7. During follow-up visit a week after discharge in the outpatients, patient did not complain of any cardiovascular disorders, bleeding symptoms, and subcutaneous hematomas presented significant involution. Laboratory findings did not reveal any abnormalities. During follow-up visit 30 days after the PCI patient presented with no cardiovascular symptoms, Echocardiographic imaging showed mild systolic LV dysfunction with EF=46%. Physical examination did not reveal any subcutaneous hematomas [Phot. 2].



Photography 1. Right arm on fifth day of hospitalization

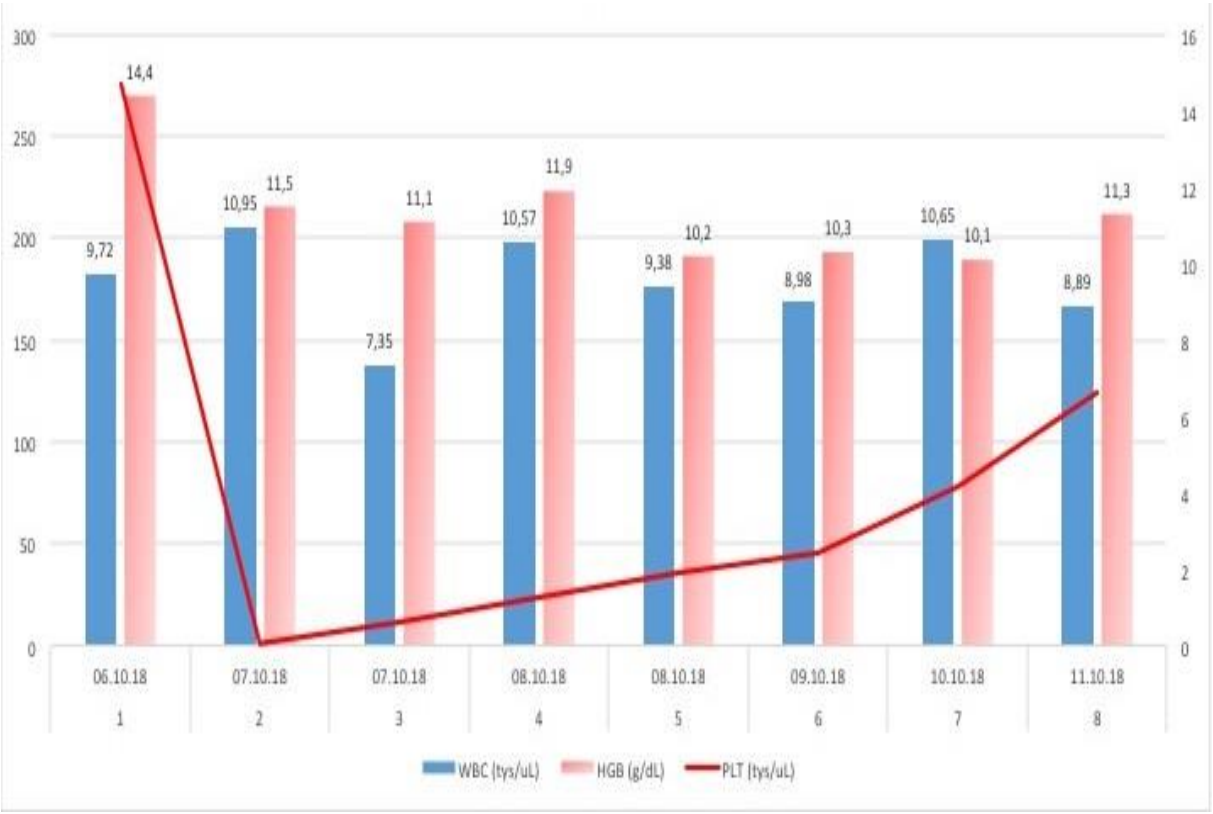
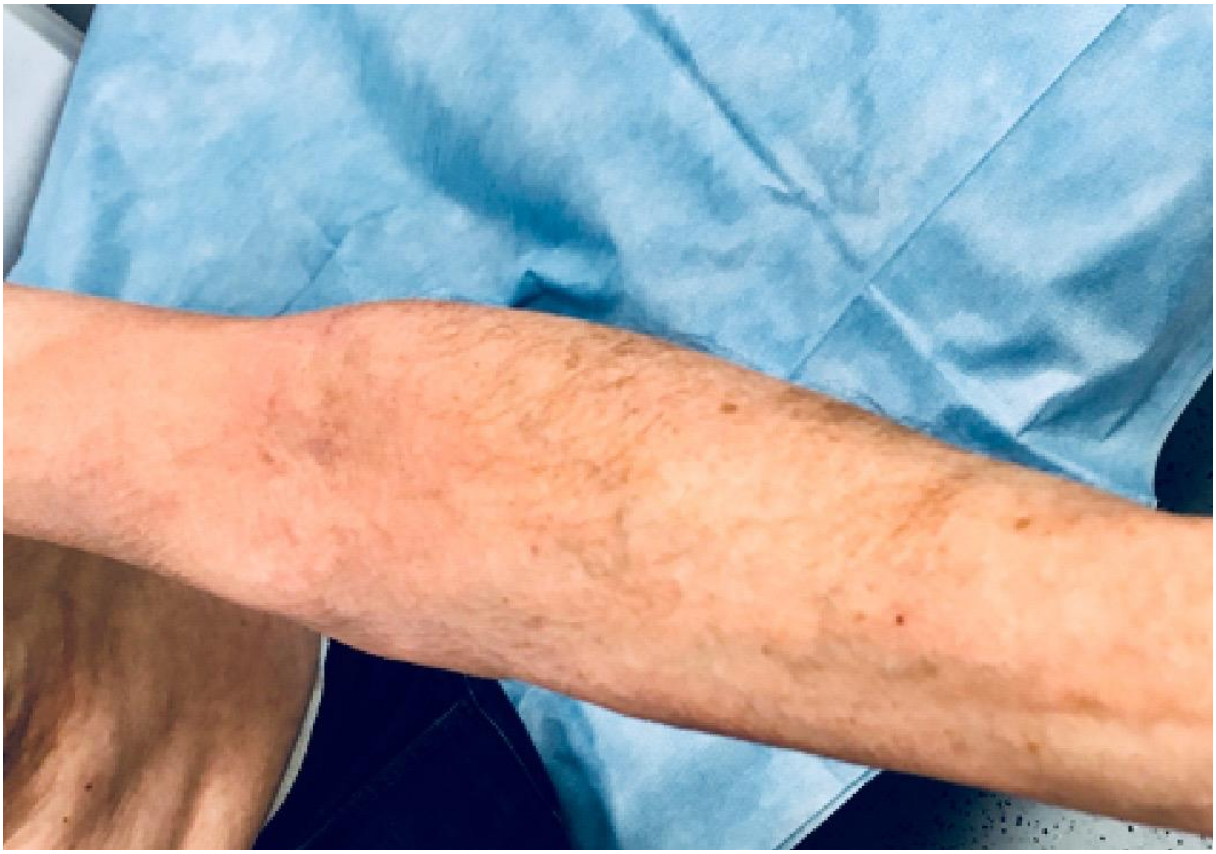


Figure 1: Changing in thrombocytes volume during hospitalization



Photography 2. Right arm on month follow-up

DISCUSSION

Glycoprotein IIb/IIIa inhibitors should be considered in case of bailout situations or thrombotic complications during percutaneous coronary interventions in the management of patients with acute coronary syndrome without persistent ST-segment elevation (NSTE-ACS) according to the ESC guidelines [1].

This case study presents a patient who required administration of eptifibatide due to slow flow phenomenon in the infarct-related artery, which significantly worsened his condition with hemodynamic instability symptoms. Taking into consideration reduced eGFR it seems advisable to consider a choice of another Gp IIb/IIIa inhibitor, nevertheless during the procedure eptifibatide was the only available Gp IIb/IIIa agent. Additionally, eGFR allowed a reduced dose of eptifibatide administration. Gp IIb/IIIa induced thrombo-cytopenia appears in 1-5.4% cases [2-5].

Independent risk factors for this complication are age > 65 y.o., low BMI, low initial PLT (<180 000/μL). Although GpIIb/IIIa induced thrombocytopenia is rarely severe, usually transient and self-limiting, with satisfactory reaction to PLT transfusion, it may result in life-threatening bleeding complications [6].

The studies prove that thrombocytopenia results from the immunological response related to drug-dependent antibodies [7-10].

In most cases drug-induced thrombocytopenia appears after few days of drug administration if a drug has previously been taken, yet in the case of Gp IIb/IIIa inhibitors may develop suddenly within few hours after the first drug administration. This could be explained with the presence of natural antibodies in these patients [7,8].

Differential diagnosis should include heparin induced thrombocytopenia. Heparin induced thrombocytopenia type I (HIT type I), is a non-immunologic response to heparin, with a mild and transient thrombocytopenia (usually below 100 000/ul), which occurs within the first 2-4 days after initiation of heparin treatment. It affects 10-20% of patients, and thrombocytopenia often returns to normal within the next few days with no further complications regardless of the continuation of heparin administration. Heparin induced thrombocytopenia type II (HIT type II) is an immune-mediated phenomenon, which usually results in platelet drop >50% (usually between 30 000–50 000/μl, however10% of patients experiences the PLT count >150 000/μL, and in 5% of patients PLT count accounts for <20 000/μL (usually in DIC), and most often appears after 4-10 days of HNF/LMWH initiation It affects 0.1-3% subjects

treated with HNF and <0.1% with LMWH and is associated with 20 – 40-fold higher thrombotic complications, which is diagnosed in 30-75% patients with HIT. Our patient experienced severe thrombocytopenia (1 000/μl) within 12h after treatment initiation, which more likely suggests GpIIb/IIIa induced thrombocytopenia than heparin-induced reaction.

CONCLUSIONS

There are particular groups of patients at risk of drug-induced thrombocytopenia, especially the elderly and those with impaired kidney function. In such cases decisions concerning treatment strategies in acute coronary syndromes should be taken cautiously, mainly concerning antiplatelet and antithrombotic medications.

Small number of patients with severe thrombocytopenia in ACS patients suggests that every case should be reported which would be helpful in the future guidelines and recommend-dations.

Moreover, such patients should undergo follow-up for further monitoring and to avoid future drug treatment.

Conflicts of interest

The authors declare no conflicts of interest.

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