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Case Report

Heparin-induced thrombocytopenia associated with polycythemia vera during the treatment of acute coronary syndrome

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ABSTRACT

Here, we report a case of heparin-induced thrombocytopenia (HIT) associated with polycythemia vera (PV) during the treatment of acute coronary syndrome. An 84-year-old woman with pre-existing PV had an acute myocardial infarction and developed HIT after using heparin. An additional myocardial infarction was caused by HIT, and caused marked damage to her cardiac function. However, she was successfully treated with argatroban infusion and intensive care. In this case, we suspected HIT at an extremely early stage, when the decline in platelet count remained at 16%, which might have prevented further thrombosis. Subsequently, the nadir in the platelet count remained at 32%, which resulted in "intermediate possibility of HIT" according to the 4Ts score; thus, further detailed serological examination may be required for accurate diagnosis of HIT.

<**Learning objective:** The main contribution of our paper is that it reveals that clinicians should exercise caution when treating patients with polycythemia vera (PV) because they are prone to serious thrombotic complications and the presence of PV may obscure the occurrence of heparin-induced thrombocytopenia because of atypical fluctuations in platelet counts. We believe that this contribution is theoretically and practically relevant because it includes findings that could enhance clinical treatment and outcomes among such patients.>

Introduction

Heparin is widely used as an anticoagulant drug during a variety of clinical situations, such as catheter intervention. Heparin-induced thrombocytopenia (HIT) is a rare, autoimmune complication of heparin that leads to thrombotic and hemorrhagic events. Approximately 0.5–3% of individuals receiving heparin develop HIT [1], which occurs 5–14 days after discontinuation of heparin treatment [2]. Thromboembolic complications of HIT are associated with high morbidity and mortality. A previous report showed that the mortality rate of HIT was approximately 15.6% [3].

We report a rare case of HIT associated with polycythemia vera (PV), during the treatment of acute coronary syndrome. Thrombosis is a common clinical feature of both HIT and PV, but the development of HIT in patients with PV is rare and under-recognized. Here, HIT was difficult to suspect and diagnose using the 4Ts score; so detailed serological investigations were essential to make an accurate diagnosis.

Case report

An 84-year-old woman, with a history of PV and cerebral infarction, presented with chest discomfort. She had been prescribed ifenprodil tartrate (60 mg/day). At admission, her vital signs were almost normal. Electrocardiography showed a normal sinus rhythm with ST elevation in V2-6, I, and aVL. Laboratory results revealed the following data: white blood cells, 31,900/μL; red blood cells, 8.39×10^6/μL; hemoglobin, 16.4 g/dL; hematocrit, 55.7%; platelets, 502×10^3/μL; creatine kinase, 407 IU/L; MB isoform, 100 IU/L; troponin I, 4.480 ng/mL; and B-type natriuretic peptide, 304.10 pg/mL. Chest radiography showed cardiomegaly (cardiothoracic ratio, 71%) and mild congestion. Chest computed tomography showed bilateral pleural effusions and spleno-hepatomegaly due to polycythemia. Transthoracic echocardiography revealed decreased left ventricular systolic function [ejection fraction (EF), 44%] with left ventricular anterior, septal, and lateral wall-motion abnormalities. Emergent coronary angiography (CAG) showed 75% stenosis of the

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left anterior descending artery (LAD) and 99% stenosis of the first large diagonal branch artery (branch #9; Fig. 1a). We planned percutaneous coronary intervention (PCI) and we administered 8000 units of heparin and started the patient on oral aspirin and prasugrel. Successful PCI was performed for branch #9 with aspiration (ThrombusterIII-GR, Kaneka, Osaka, Japan) and balloon angioplasty (SeQuent, B-Brawn, Melsungen, Germany), without any stent implantation. The final CAG finding after PCI is shown in Fig. 1b.

After PCI, the patient's condition improved and her chest pain resolved. However, on the 9th day from admission, she experienced chest oppression and dyspnea. After we injected 2000 units of heparin, repeat CAG was performed, but no obstructions were seen via CAG. On the 12th day from admission, we planned PCI for 75% stenosis of the LAD to control heart failure and its symptoms. After we injected 8000 units of heparin, we began PCI and inserted guidewire for the LAD. After the observation by intravascular ultrasound system (IVUS; View IT, Terumo, Tokyo, Japan) for the LAD, which showed no thrombi in the LAD, the patient began to experience chest discomfort and we identified ST elevation in V2-6, I, and aVL. CAG revealed numerous thrombi in multiple vessels, in not only the LAD, but also branch #9 (Fig. 1c). We examined the activated clotting time (ACT) and confirmed that it was within the therapeutic range (300 s). Although platelet counts barely decreased, the unexplained thrombus formation suggested HIT. We switched anticoagulant treatment from heparin to argatroban, after which all thrombi dissipated (Fig. 1d). However, the patient's left ventricular function was badly damaged (EF = 30%) and she suffered from heart failure due to cardiac pump dysfunction. She received intensive treatments, including non-invasive positive airway ventilation, dobutamine, norepinephrine, and anticoagulation therapy with intravenous infusion of argatroban.

On the 13th day from admission, the patient tested positive for heparin-platelet factor 4 complex antibody (HIT-antibody, 3.6 U/mL; cut off <1.0 U/mL; BML Inc., Tokyo, Japan). We deemed further investigation necessary to diagnose HIT accurately; therefore, we sent the patient's serum to a highly advanced medical facility: the National Cardiovascular Center Laboratories, Suita, Osaka, Japan. The results of further confirmatory tests were all positive (OD of IgG HIT-antibody, 0.839, cut off <0.4; functional assay of HIT-antibody, positive).

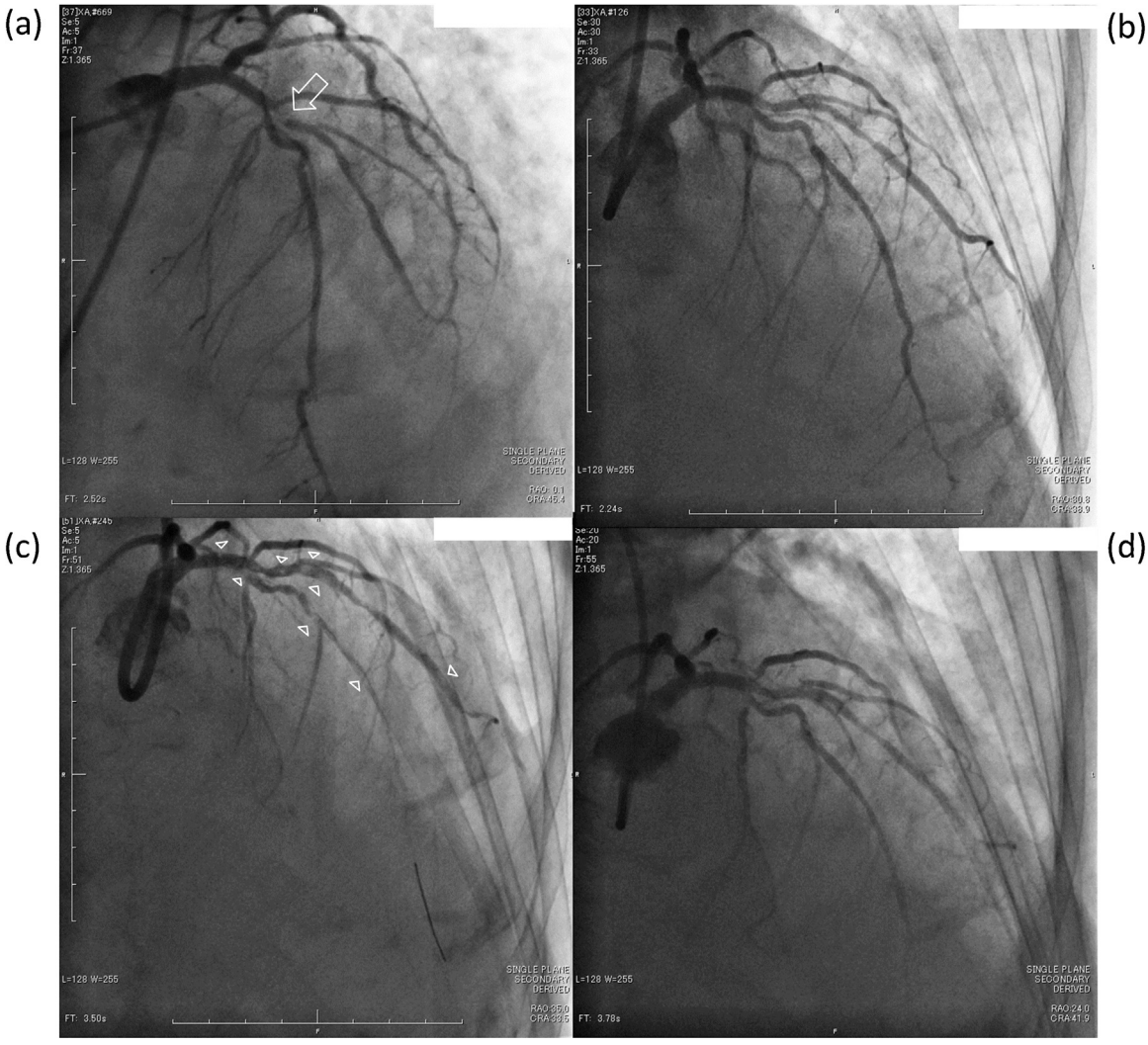

Fig. 1. (a) Emergent coronary angiography (CAG) performed on admission. Arrow indicates the 99% stenosis of the first large diagonal branch artery (#9). (b) After the successful percutaneous coronary intervention (PCI) for #9, there were no thrombi and no flow limitations in coronary artery. (c) During the second PCI, CAG revealed numerous thrombi, in multiple vessels. Triangles indicate the thrombi. The flow limitation of the left anterior descending artery (LAD) was observed because of the thrombi. (d) After we ceased use of heparin and reinstituted argatroban treatment, the thrombi in the coronary artery almost completely dissipated and the flow of the LAD was gradually restored.