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Case Report

A case of heparin-induced thrombocytopenia with subacute stent thrombosis, multiple cerebral infarction, and acute limb ischemia

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ABSTRACT

Heparin-induced thrombocytopenia (HIT) is an adverse immune-mediated drug reaction that is associated with thromboembolic complications. We report the case of an 82-year-old man with unstable angina pectoris who suffered from recurrent arterial thromboembolism due to HIT. Coronary angiography (CAG) was performed while we administered unfractionated heparin bolus. CAG showed triple-vessel disease without left main coronary artery. We performed elective percutaneous coronary angioplasty (PCI) to the left anterior descending coronary artery (LAD). The sudden thrombus formation in the LAD occurred during the procedure. We suspected HIT and administered argatroban. We deployed four everolimus-eluting stents in the LAD and intra-aortic balloon pumping (IABP) support was started. The platelet counts were rapidly reduced almost 50% next day after PCI and IgG-specific anti-PF4/heparin antibodies were elevated. Multiple cerebral infarctions were detected by magnetic resonance imaging after the PCI. The patient received the continuous argatroban administration and IABP support for 4 days. Subacute stent thrombosis occurred after quitting argatroban. We performed thrombus aspiration and fibrinolytic treatment. Finally we re-inserted IABP and stabilized the hemodynamic state. Right popliteal arterial thromboembolism occurred after emergency PCI. Argatroban is essential and following oral anticoagulant therapy is necessary to prevent thromboembolic complications.

<**Learning objective:** Heparin-induced thrombocytopenia (HIT) is an adverse immune-mediated drug reaction that is associated with thromboembolic complications. The incidence of HIT in patients who received unfractionated heparin is reported to be 0.1– 1%. We should be aware of HIT when thromboembolic complications occur during the percutaneous coronary intervention procedure. Argatroban is essential and following oral anticoagulant therapy is necessary to prevent thromboembolic complications among patients with HIT.>

Introduction

Heparin-induced thrombocytopenia (HIT) is an adverse immune-mediated drug reaction that is associated with thromboembolic complications. Heparin exposure leads to the formation of IgG antibodies that recognize platelet factor 4 (PF4) and heparin complex. These complexes bind to the Fcγ receptors of platelets resulting in platelet activation and thrombus formation. The incidence of HIT in medical patients who received unfractionated heparin (UFH) is reported to be 0.1–1% and the incidence of thrombotic events is approximately 50% of patients confirmed with HIT [1,2]. Venous thromboembolism (VTE) is the most frequent complication of HIT. Arterial thrombotic events also occur but less often than VTE. Stent thrombosis is a rare but frequently fatal complication of percutaneous coronary intervention (PCI). A recent large-scale registry shows that the rate of early stent

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thrombosis is <1% with modern generation drug-eluting stents (DES) [3].

We here report our case that experienced arterial thrombotic events including all of the following: coronary artery thrombosis, multiple cerebral infarctions, subacute stent thrombosis, and peripheral arterial thrombosis in the same admission period due to HIT. The patient survived having been administered continuous intravenous argatroban followed by treatment with oral warfarin.

Case report

An 82-year-old man was referred to our emergency department with chest pain. An electrocardiogram showed ST segment depression in II, III, aV_F, and V3 to 6 leads and serum troponin T level did not increase, which suggested unstable angina pectoris (UA). We started continuous intravenous administration of UFH and isosorbide dinitrate (ISDN). After treatment, the chest pain diminished and ST depression was resolved. Continuous intravenous administration of UFH was withdrawn on the 9th hospital day and elective coronary angiography (CAG) was performed with UFH 2000 units bolus on the 17th hospital day (Fig. 1). CAG showed 75% stenosis of the mid left anterior descending coronary artery (LAD), the proximal left circumflex coronary artery (LCX), and the distal right coronary artery. CAG showed triple-vessel disease without left main coronary artery and we decided to perform elective PCI to the LAD. The patient was given aspirin 100 mg from the admission date and clopidogrel 75 mg was started after CAG.

On the 25th hospital day we performed elective PCI to the LAD. Intravenous bolus dose of 5000 units of UFH was administered prior to the PCI procedure. During the intravascular ultrasound (IVUS) procedure to the LAD before stent deployment, the patient complained of chest pain and ST-segment in the precordial leads was elevated. We performed pre-dilatation with 2.0 mm balloon and deployed a 2.5 mm × 28 mm platinum chromium everolimus-eluting Stent (PtCr-EES) (Promus PREMIER™, Boston Scientific, Nattick, MA) to the LAD (Fig. 2A). After stent deployment, slow flow phenomenon occurred at the midportion of the LAD (Fig. 2B). IVUS revealed the stent malapposition in the proximal portion of the deployed stent and thrombus formation. We performed post dilatation with 2.5 mm balloon and deployed 2.5 mm × 16 mm PtCr-EES (Promus PREMIER™) in the proximal part of the LAD. After stent deployment, the proximal stent looked hazy and we checked activated coagulation time (ACT) which was 308 s. We suspected HIT and administered argatroban bolus. We deployed another 2 stents to cover the proximal part of the LAD; a 2.5 mm × 16 mm cobalt–chromium everolimus-eluting stent (CoCr-EES) (Xience Xpedition ®, Abbott Vascular, Santa Clara, CA, USA) and a 3.0 mm × 12 mm PtCr-EES (Promus PREMIER™). After stent deployment, slow flow phenomenon occurred again. Despite repeated thrombus aspiration and balloon dilatation, the coronary flow was not restored. Finally we inserted the intra-aortic balloon pumping (IABP).The platelet counts were rapidly reduced from 257×10^9 per L to 140×10^9 per L next day after PCI. We ceased UFH and started continuous argatroban administration. We adjusted the dose of argatroban to maintain activated partial thromboplastin time (aPTT) between 1.5–3 times of the patient baseline according to the guidelines of the American College of Chest Physicians (ACCP) [2]. The platelet counts gradually increased after the elective PCI (Fig. 1). Four days after the PCI, on the 29th hospital day, we removed IABP and withdrew the continuous argatroban administration. On the 33rd hospital day, 3 days after we quit continuous argatroban administration, multiple cerebral infarctions were detected by magnetic resonance imaging (Fig. 2C). The diagnosis of HIT was confirmed by the anti-platelet factor (PF) 4/heparin enzyme immunoassay and the functional test. Optical density values for IgG-specificanti-PF4/heparin antibodies were 2.459, which indicated immunoassay test was strongly positive (optical density value >1.5). The washed platelet activation assay using flow cytometry according to the previous publication was also performed [4]. An obvious release of microparticle was detected when the patient's serum was added to heparin-infused washed platelet concentrates, which indicated the functional assay was positive. The 4Ts Score, which is widely used for evaluating the present probability of HIT, was 6 points

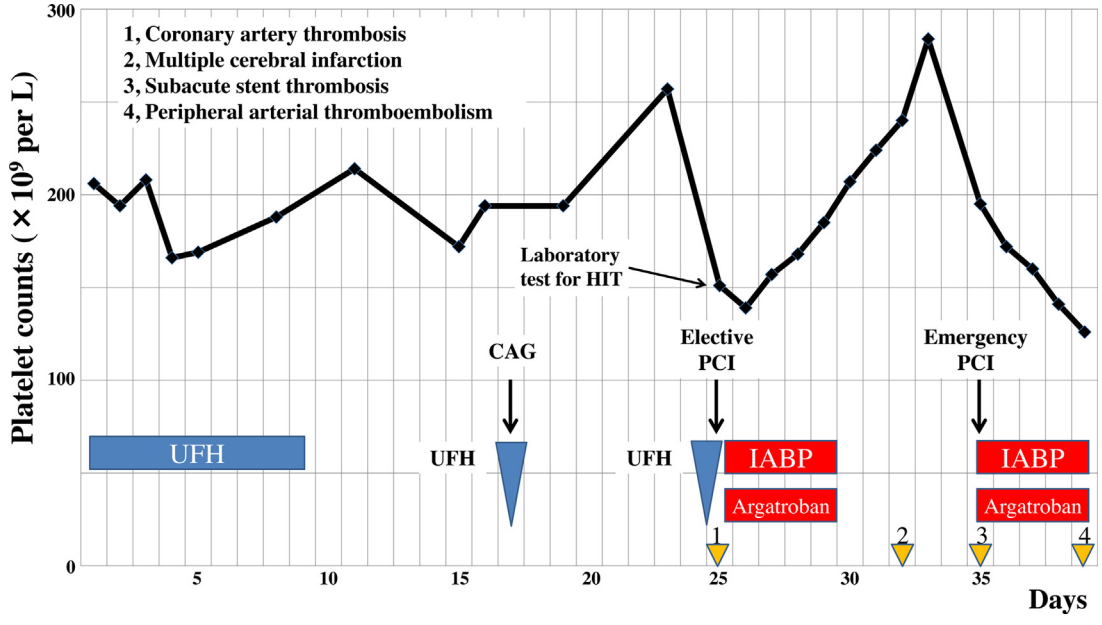

Fig. 1. Clinical course after admission to our hospital. We performed coronary angiography (CAG) on the 17th hospital day. On the 25th hospital day, we performed the elective percutaneous coronary intervention (PCI) to the left anterior descending coronary artery. On the 35th hospital day, subacute stent thrombosis occurred and we performed emergency PCI.
HIT, heparin-induced thrombocytopenia; UFH, unfractionated heparin; IABP, intra-aortic balloon pumping.

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