Case Report

http://dx.doi.org/10.4070/kcj.2012.42.9.646
Print ISSN 1738-5520 • On-line ISSN 1738-5555

kcj
Korean Circulation Journal

Acute Stent Thrombosis and Heparin Induced Thrombocytopenia in a Patient With ST-Segment Elevation Myocardial Infarction

Hong Won Shin, MD, Hyuck Jun Yoon, MD, Sang Woong Choi, MD, Han Jun Bae, MD, Ji Hyun Sohn, MD, Ho Myung Lee, MD, Hyun Ok Cho, MD, Yun Kyeong Cho, MD, Hyoung Seob Park, MD, Hyungseop Kim, MD, Chang Wook Nam, MD, Seung Ho Hur, MD, Yoon Nyun Kim, MD, and Kwon Bae Kim, MD

Division of Cardiology, Department of Internal Medicine, Dongsan Medical Center, Keimyung University College of Medicine, Daegu, Korea

Heparin is an essential drug in the treatment of acute coronary syndrome and it is used during percutaneous coronary intervention (PCI). Heparin-induced thrombocytopenia (HIT), albeit a serious complication of heparin therapy characterized by thrombocytopenia and high risk for venous and arterial thrombosis, has rarely been previously reported during PCI. We report a case of an acute stent thrombosis due to an unusual cause, HIT during primary PCI, in a patient with acute myocardial infarction. **(Korean Circ J 2012;42:646-649)**

KEY WORDS: Heparin; Thrombocytopenia; Thrombosis; Myocardial infarction.

Introduction

The incidence of stent thrombosis (ST) is relatively rare, with reported rates around 1-2%; however its consequences can be fatal, as most ST cases are associated with myocardial infarction or sudden death.[1] In accordance with the Academic Research Consortium definition, ST was subdivided into early ST (0 to 30 days), late ST (31 to 360 days), and very late ST (>360 days). Acute ST was defined as occurring during the 24 hours after the intervention.[2][3] Early ST may be related to residual target lesion thrombus or dissection, stasis, stent underexpansion, or a combination of these.[4]

It is recommended for patients proceeding to primary percutaneous coronary intervention (PCI) with ST-segment elevation myocardial infarction (STEMI) to be given supportive anticoagulant regimens such as unfractionated heparin (UFH).[5] However ST, during coronary angioplasty in association with the abrupt onset of heparin induced thrombocytopenia (HIT), has rarely been reported previously.[6] Further, we here report a case of the acute ST due to HIT during primary PCI.

Received: January 18, 2012
Revision Received: February 1, 2012
Accepted: February 6, 2012
Correspondence: Hyuck Jun Yoon, MD, Division of Cardiology, Department of Internal Medicine, Dongsan Medical Center, Keimyung University College of Medicine, 56 Dalseong-ro, Jung-gu, Daegu 700-712, Korea
Tel: 82-53-250-7448, Fax: 82-53-250-7034
E-mail: hippsons@dsmc.or.kr

• The authors have no financial conflicts of interest.

Case

A 62-year-old woman was admitted with resting chest pain for 5 hours. As a cardiovascular risk factor, she had a history of type 2 diabetes mellitus for 5 years. The initial electrocardiogram showed ST-segment elevation in II, III, and aVF. She was given aspirin 300 mg, clopidogrel 600 mg and UFH 3600 unit loading dose, and continuous UFH was injected for at a maintenance rate of 12 unit/kg/hour according to American College of Cardiology/American Heart Association guideline.[7] With the diagnosis of STEMI, she was sent to cardiac catheterization laboratory. Right coronary angiogram revealed total occlusion of the mid portion of the right coronary artery (RCA) with thrombus (Fig. 1A). Left coronary angiogram also showed a tight stenotic lesion in the mid portion of the left anterior descending artery (LAD, 65%) and left circumflex artery (LCX, 85%). We planned primary PCI at RCA as infarct-related artery and secondary PCI on LAD and LCX. We dilated the mid RCA lesion using a 2.0×15 mm balloon. Thereafter, abundant thrombus was shown in the middle to distal RCA and thrombus aspiration was performed; a 2.75×33 mm everdimus-eluting stent (Xience Prime™, Abbott, Santa Clara, CA, USA) was deployed at 10 atmospheres in the mid RCA. After stent deployment, thrombus was shown at proximal end of the st-

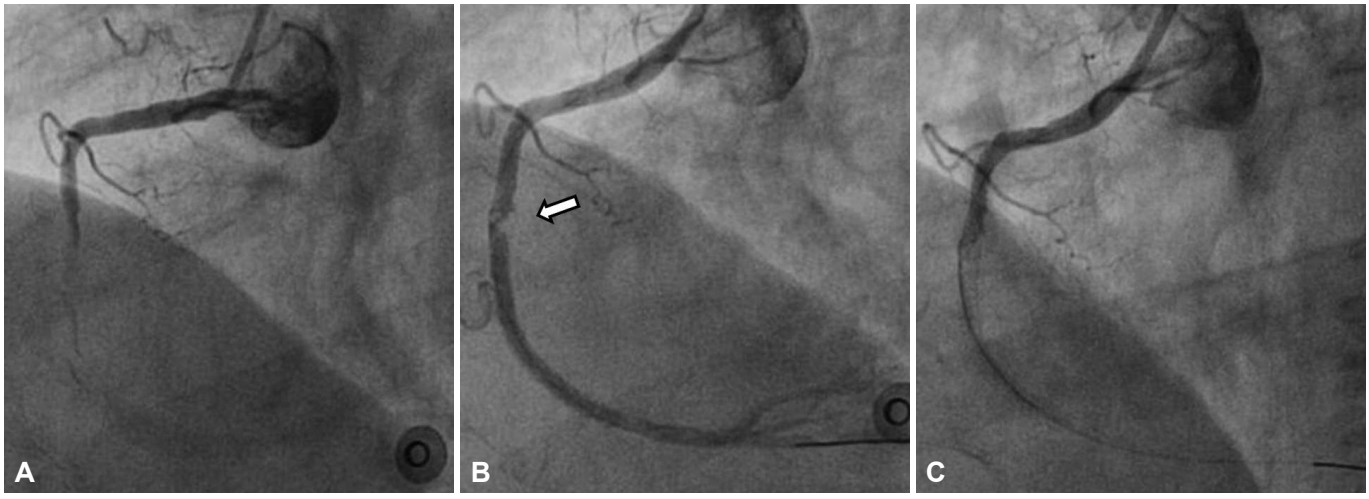

Fig. 1. Coronary angiogram demonstrated acute stent thrombosis during primary percutaneous coronary intervention. A: initial coronary angiogram revealed total occlusion of the mid portion of the right coronary artery (RCA) with thrombus. B: after stent deployment, thrombus (arrow) was shown at proximal portion of the stent. C: a few minutes after, it showed complete occlusion of the mid RCA stent site with progressed thormbus from the proximal portion of RCA.

ent (Fig. 1B). We did thrombus aspiration and additional balloon dilatation; however, angiogram showed complete occlusion of the mid RCA stent site with progressed thrombus from the proximal portion of RCA (Fig. 1C). The activated clotting time (ACT) was 239 seconds at that time. Despite repeated thrombus aspiration and balloon dilatation, coronary flow was not restored. We checked intravascular ultrasound (IVUS) on this site to exclude another reason to compromise coronary flow, such as edge dissection or underexpansion. In IVUS, there was total occlusion by extensive thrombus in RCA; however, there was no evidence of edge dissection, stent malapposition or underexpasion (Fig. 2). A bolus dose of glycoprotein IIb/IIIa receptor antagonist abciximab (2.5 mg/kg) was given into the RCA followed by continuous infusion (0.125 mcg/kg/min). The RCA flow was not restored despite repeated efforts, and thrombus further progressed proximal to the stented area. We scheduled delayed PCI on RCA and non-culprit lesion on LAD and LCX, after medical treatment.

As compared to the admission platelet count of 443000/mm^3, a repeat platelet count 6 hours after PCI was 158000/mm^3 and even further decreased to 4000/mm^3 at 2 days after PCI. Aspirin, clopidogrel, abciximab and UFH were discontinued after a repeat count in an ethylenediaminetetraacetic acid-free citrate tube confirmed the finding. We used a clinical scoring system for identifying those with HIT.[8] The patient had thrombocytopenia, proven new thrombosis, and timing of onset of platelet fall was under 1 day. Further, there was no other cause for the platelet count fall. Thus, we diagnosed heparin induced thrombocytopenia and administered the direct thrombin inhibitor, argatroban (2 μg/kg/min). Two units of platelets were transfused, due to bleeding concerns and profound thrombocytopenia. Post-transfusion platelet count was 7000/mm^3 and a few hours later dropped to 5000/mm^3, but stabilized at 855000/mm^3 at

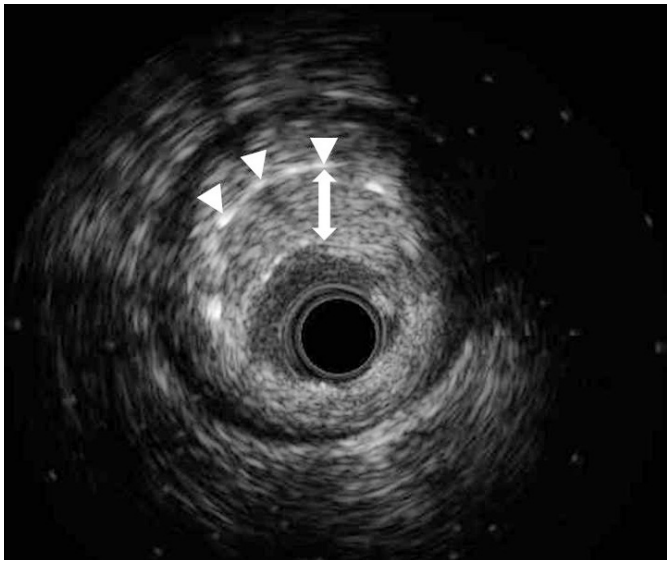

Fig. 2. In intravascular ultrasound on right coronary artery after stent deployment, there was total occlusion by extensive thrombus and there was no evidence of edge dissection, incomplete stent apposition or underexpansion (arrow heads showed stent struts and arrow showed thrombus).

5 days after PCI, at which time, aspirin and clopidogrel were reinitiated and argatroban was discontinued.

Eleven days after admission, secondary PCI was performed using argatroban targeting ACT to 250-400 seconds. At that time, we used heparin free flushing solution to avoid recurrent heparin induced thrombocytopenia. Right coronary angiogram revealed total occlusion from the RCA ostium (Fig. 3A). The RCA totally occluded lesion was successfully crossed after several attempts and balloon angioplasty was performed using a 2.5 mm balloon. Despite repeated balloon inflation and thrombus aspiration, RCA thrombolysis in myocardial infarction 3 flow could not be achieved (Fig. 3B). At the

http://dx.doi.org/10.4070/kcj.2012.42.9.646

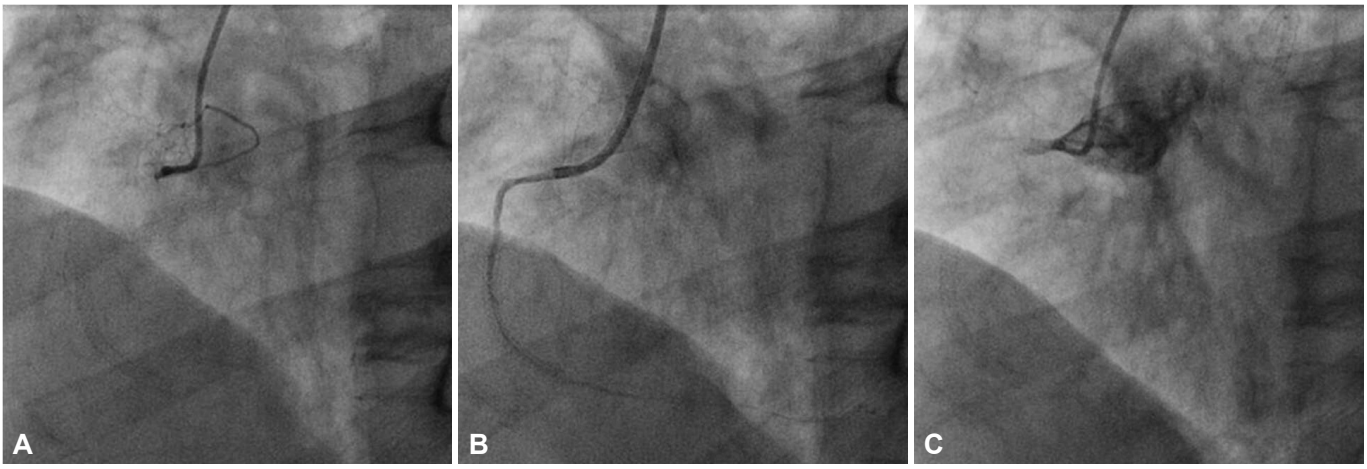

Fig. 3. Follow up coronary angiogram demonstrated persistent stent thrombosis. A: secondary stage coronary angiogram showed more progressed intracoronary thrombosis from RCA ostium. B: despite repeated balloon and thrombus aspiration Thrombolysis in Myocardial Infarction 3 flow could not be obtained. C: a few minute after, coronary flow of RCA was disappeared. RCA: right coronary artery.

LAD and LCX, 2.75×38 mm and 2.75×18 mm everolimus-eluting stents (XIENCE PRIME™ Abbott) were deployed, respectively. After left coronary PCI, a repeated right coronary angiogram was performed. It showed disappearance of the previously shallow coronary flow and we did not perform any further procedures in the RCA (Fig. 3C).

After the second PCI, platelet count was not decreased and the patient was subsequently discharged with a platelet count of 427000/mm^3. There was no evidence of aspirin or clopidogrel resistance. Although there are concerns of increased bleeding risk from triple therapy, our patient was discharged on aspirin, clopidogrel and warfarin.

Discussion

Heparin induced thrombocytopenia carries a significant risk for venous and arterial thrombotic events. Very rarely, it has been described in the setting of coronary angioplasty for an acute myocardial infarction in association with the abrupt onset of HIT, such as in this case.[6)9)10)]

Heparin induced thrombocytopenia is a prothrombotic disorder initiated by heparin administration and is related to antibody-mediated platelet activation, causing thrombin generation and thrombotic complications. HIT can be regarded as a severe adverse drug reaction resulting from multicellular immune activation.[11)] The diagnosis of HIT is based on its typical clinical feature. The '4Ts' of HIT refers to the degree of Thrombocytopenia, the Timing of the platelet fall after heparin exposure, the presence of Thrombosis, and oTher causes for thrombocytopenia excluded.[8)] UFH has been the traditional antithrombin agent during PCI. The American College of Cardiology recommends the use of UFH during PCI, with the dose adjusted for ACT (Class I, Level of Evidence: C), or enoxaparin (Class IIa, Level of Evidence: B).[12)]

In patients with HIT, heparin should be avoided to prevent recurrent HIT and PCI should be performed using alternative anticoagulants, despite the fact that their safety and efficacy have not been established.[13)] Direct thrombin inhibitors, such as argatroban, bivalirudin, and hirudin, offer the theoretical advantages of inhibition of soluble and bound thrombin, ease of titration, and rapid reversal of anticoagulant effects upon cessation of therapy, without cross-reactivity with HIT antibodies.[14)] Argatroban is approved to treat both HIT complicated by thrombosis and isolated HIT. Lewis et al.[15)] reported that 91 HIT patients underwent 112 separate coronary interventions on 177 lesions using argatroban anticoagulation, and satisfactory outcome of the procedure was attained in 94.5%. They reported that argatroban enabled satisfactory outcomes of procedures and provided adequate anticoagulation for HIT patients undergoing PCI on single or multiple occasions. The anticoagulatory effects of argatroban and UFH were obtained with comparable safety, since there were no significant differences in angiographic success rates, PCI-induced troponin level elevation, occurrence of the composite endpoint of death, MI, or revascularization, as well as incidence of bleeding events.[16)] Argatroban dose-dependently increases coagulation parameters and compared to UFH, demonstrates a superior predictable anticoagulant effect in patients undergoing elective PCI.[16)]

This case report offers several unknowns. Several risk factors implicated in acute ST were present in our patient, such as multivessel disease, PCI in the setting of acute coronary syndrome, and diabetes mellitus. Moreover, acute ST is reported in up to 0.5-0.7% of the cases in the first 24 hours post PCI.[17)] Abciximab, which is a potent inhibitor of platelet aggregation, can also induce thrombocy-

topenia within 24 hours of first exposure.[9] The exposure to abciximab can result in a more rapid, severe thrombocytopenia in HIT. In our case, abciximab was given after ST. Therefore, we do not consider its cause. Although profound thrombocytopenia could have been an effect of abciximab, an acute ST with thrombus during PCI may account for HIT.[17]

Stent thrombosis was affected by various factors. This case shows that HIT could be one of the causes of acute ST. Prompt identification and management of acute ST with HIT is critically important to avoid serious complications.

References

1. Iakovou I, Schmidt T, Bonizzoni E, et al. Incidence, predictors, and outcome of thrombosis after successful implantation of drug-eluting stents. *JAMA* 2005;293:2126-30.
2. Mauri L, Hsieh WH, Massaro JM, Ho KK, D'Agostino R, Cutlip DE. Stent thrombosis in randomized clinical trials of drug-eluting stents. *N Engl J Med* 2007;356:1020-9.
3. Wenaweser P, Rey C, Eberli FR, et al. Stent thrombosis following bare-metal stent implantation: success of emergency percutaneous coronary intervention and predictors of adverse outcome. *Eur Heart J* 2005; 26:1180-7.
4. Fujii K, Carlier SG, Mintz GS, et al. Stent underexpansion and residual reference segment stenosis are related to stent thrombosis after sirolimus-eluting stent implantation: an intravascular ultrasound study. *J Am Coll Cardiol* 2005;45:995-8.
5. King SB 3rd. 2009 update of the ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction and guidelines on percutaneous coronary intervention: what should we change in clinical practice? *Pol Arch Med Wewn* 2010;120:6-8.
6. Gupta BK, Savage MP, Brest AN. Acute myocardial infarction during coronary angioplasty associated with heparin-induced thrombocytopenia. *Cathet Cardiovasc Diagn* 1995;35:42-6.
7. Antman EM, Anbe DT, Armstrong PW, et al. ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction--executive summary. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to revise the 1999 guidelines for the management of patients with acute myocardial infarction). *J Am Coll Cardiol* 2004;44: 671-719.
8. Babuin L, Pengo V. Argatroban in the management of heparin-induced thrombocytopenia. *Vasc Health Risk Manag* 2010;6:813-9.
9. Dasari TW, Pappy R, Hennebry TA. Acute stent thrombosis associated with heparin-induced thrombocytopenia and abciximab-induced profound thrombocytopenia. *J Invasive Cardiol* 2011;23:E5-8.
10. Hussain F, Philipp R, Zieroth S. HITT and stent thrombosis: a "clinical" diagnosis not to be missed. *Int J Cardiol* 2009;133:e11-3.
11. Warkentin TE. Heparin-induced thrombocytopenia: pathogenesis and management. *Br J Haematol* 2003;121:535-55.
12. Smith SC Jr, Feldman TE, Hirshfeld JW Jr, et al. ACC/AHA/SCAI 2005 guideline update for percutaneous coronary intervention--summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/SCAI Writing Committee to update the 2001 Guidelines for Percutaneous Coronary Intervention). *Catheter Cardiovasc Interv* 2006;67:87-112.
13. Matsue H, Masai T, Yoshikawa Y, Kawamura M. Serious acute coronary thrombosis associated with heparin-induced thrombocytopenia in off-pump coronary artery bypass grafting. *Interact Cardiovasc Thorac Surg* 2010;11:188-90.
14. Brieger DB, Mak KH, Kottke-Marchant K, Topol EJ. Heparin-induced thrombocytopenia. *J Am Coll Cardiol* 1998;31:1449-59.
15. Lewis BE, Matthai WH Jr, Cohen M, Moses JW, Hursting MJ, Leya F. Argatroban anticoagulation during percutaneous coronary intervention in patients with heparin-induced thrombocytopenia. *Catheter Cardiovasc Interv* 2002;57:177-84.
16. Rössig L, Genth-Zotz S, Rau M, et al. Argatroban for elective percutaneous coronary intervention: the ARG-E04 multi-center study. *Int J Cardiol* 2011;148:214-9.
17. Van Werkum JW, Heestermans AA, Zomer AC, et al. Predictors of coronary stent thrombosis: the Dutch Stent Thrombosis Registry. *J Am Coll Cardiol* 2009;53:1399-409.

 http://dx.doi.org/10.4070/kcj.2012.42.9.646