CASE REPORT
Korean Circulation J 2006;36:324-327
ISSN 1738-5520

Late Late Stent Thrombosis after Intracoronary Brachytherapy: Learning from Brachytherapy Experiences in the Drug-Eluting Stent Era

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ABSTRACT

Stent thrombosis is generally a fatal complication after percutaneous coronary intervention. Combined antiplatelet therapy is recommended to prevent stent thrombosis in those patients who have undergone stenting. However, there are conflicting opinions on the appropriate duration of instituting antiplatelet treatment, especially after intracoronary radiation therapy or drug-eluting stent implantation, which are two situations closely associated with an increased risk of stent thrombosis. We report here on 2 cases of late stent thrombosis that occurred despite giving combined antiplatelet therapy, and these maladies developed more than 4 years after intracoronary brachytherapy. **(Korean Circulation J 2006;36:324-327)**

KEY WORDS : Angioplasty ; Stents ; Radiotherapy ; Coronary thrombosis.

Introduction

Combined antiplatelet therapy has dramatically reduced the incidence of stent thrombosis, which is one of the most feared complications and major pitfalls of stenting.[1)] The recommended duration of combined antiplatelet therapy has been extended from four weeks to more than six months after the published reports of late thrombosis and the consequent late adverse outcomes after conducting intracoronary radiation therapy or drug-eluting stent (DES) implantation.[1-3)]

Late stent thrombosis (LST) is usually defined as any stent thrombosis that occurs beyond 30 days after percutaneous coronary intervention, and this often results in a fatal acute coronary event.[2)4)5)] The risk of LST is known to dramatically increase after intracoronary irradiation; therefore, the prolonged use of antiplatelet agents for more than 12 months is the recommended therapy for stented patients who have undergone brachytherapy.[6)7)] LST after brachytherapy is postulated to be related to the delayed reendothelialization or endothelial dysfunction.[4)8)] The term 'late late stent thrombosis' (late LST) was proposed for the patients who still have a patent treatment site at 6 months and they subsequently develop a total occlusion.[9)]

We report here on 2 cases of late LST that occurred despite combined antiplatelet therapy, and these maladies developed 4 years after the patients underwent brachytherapy. Both cases presented as acute myocardial infarction and both had fatal outcomes.

Received : October 21, 2005
Revision Received : November 2, 2005
Accepted : November 5, 2005
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Case

Case 1:

In April 1999, a 46 year-old man was found to have developed in-stent restenosis (ISR) of a bare metal stent (Microstent, 3.0×24 mm, Arterial Vascular Engineering, US) that was implanted in the proximal left anterior descending coronary artery (LAD) (Fig. 1A). This 30 pack-year smoker had a history of hypertension, coronary bypass surgery and coronary stenting of his native vessels due to graft stenoses.

After performing rotablation for the ISR lesion and following this with stent insertion (NIR stent, 3.0×9 mm,

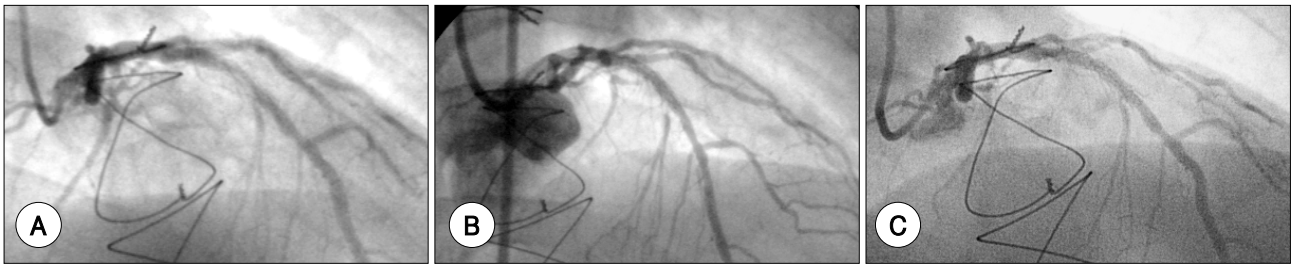

Fig. 1. Initial, post-procedural and follow-up angiograms of case 1. A: in-stent restenosis of the bare metal stent in the proximal left anterior descending artery. B: post-procedural angiogram after performing intracoronary brachytherapy. C: patent previous intervention site at 29 months after the brachytherapy.

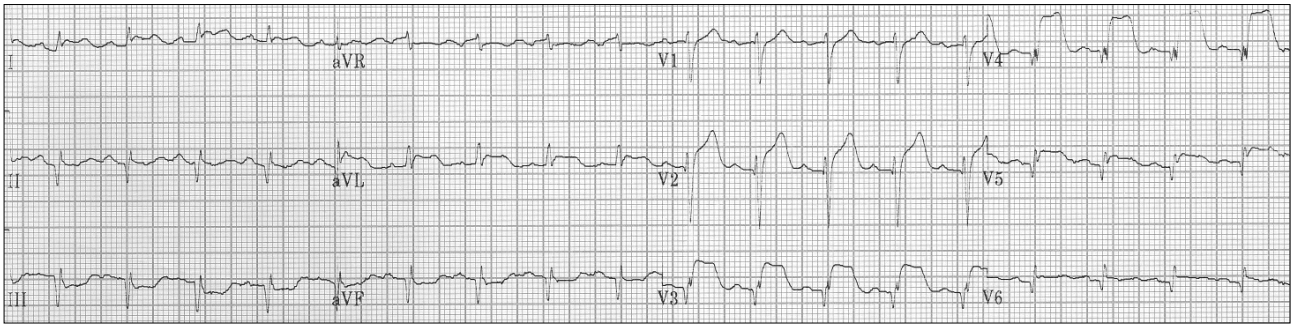

Fig. 2. Electrocardiogram taken at the emergency room showed ST elevation in V2-6, lead I and aVL, and this indicated anterolateral wall acute myocardial infarction. ST: stent thrombosis.

Boston Scientific, US), intracoronary irradiation was performed for 25.5 minutes by employing the ^{188}rhenium-filled angioplasty balloon catheter system (Maxxum, 3.0×30 mm, Scimed/Boston Scientific, US), and with using a similar method as was previously reported (Fig. 1B).[10][11] He was discharged in stable condition and medicated with antihypertensives, aspirin 100 mg qd and ticlopidine 250 mg bid.

Six, twelve and twenty-nine months after brachytherapy, the patient underwent follow-up coronary angiographies; these procedures showed persistent optimal results in the irradiated coronary artery (Fig. 1C). Ticlopidine was given for the first year, and then it was discontinued thereafter, while the aspirin was continued. Cilostazol was added at the 29 months follow-up.

In October 2003 (54 months after the brachytherapy), the patient presented to the emergency room with sudden chest pain and he was diagnosed as having ST-elevation acute myocardial infarction (Fig. 2). An emergency coronary angiography revealed a total occlusion in the previously irradiated proximal LAD stent site (Fig. 3). Performing immediate balloon angioplasty showed TIMI grade II antegrade flow and a large in-stent thrombi. After aspiration of the thrombi with using a PercuSurge GuardWire™ (Medtronic, US) (Fig. 3, box) and giving an abciximab infusion, we implanted a taxol-eluting stent (Taxus, 3.5×16 mm, Boston Scientific, Ireland). At the end of the intervention, an intraaortic balloon pump (IABP) was inserted for instituting hemodynamic support.

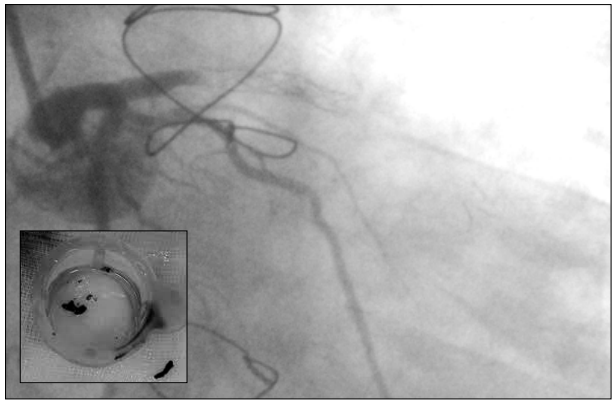

Fig. 3. Total occlusion of the proximal left anterior descending artery stent site (54 months after brachytherapy) and the aspirated thrombi (box).

In the intensive care unit, the patient suffered from prolonged hypotension despite the successful intervention and full hemodynamic support with inotropics and IABP. Despite our strenuous efforts, he expired from respiratory failure due to pneumonia and pulmonary edema.

Case 2:

A 73 year-old man with a 25 pack-year history of smoking presented to us with exertional chest pain and dyspnea. He was being treated with antihypertensive medication and he had a positive treadmill test. Coronary angiography showed an occlusive lesion at the mid right coronary artery (RCA), and so a stent (GFX, 3×18 mm,

Arterial Vascular Engineering, US) was implan-ted.

At the 6 month follow-up, we found a tight stenosis at the proximal edge of the RCA stent. The lesion was treated with a stent (NIR stent, 3.0×9 mm, Boston Scientific, US), and this was followed by intracoronary irradiation with using a ^{188}rhenium-filled angioplasty balloon catheter system (Adante, 3.0×20 mm, Scimed/Boston Scientific, US, 12 minutes).

Aspirin and ticlopidine were prescribed for 2 months, and only the aspirin was continued thereafter. Cilostazol was added 12 months after the intervention.

At 6 months and 23 months after brachytherapy, there was no evidence of restenosis in the irradiated lesion, and there were no specific cardiac symptoms.

In December 2003 (49 months after brachytherapy), the patient presented to the emergency room suffering with general weakness and sweating. Upon arrival, the ECG showed ST elevations in leads II, III and aVF; this was a consistent finding along with the acute inferior wall myocardial infarction.

Performing emergency coronary angiography with IABP and a temporary pacemaker revealed a total occlusion in the mid-RCA with in-stent thrombi. The thrombi were aspirated with using a PercuSurge GuardWire™ (Medtronic, US), and stents were then implanted (Taxus 3×32 mm, 2.75×32 mm, Boston Scientific, Ireland).

Despite the intervention and being treated with full supportive care, the patient died of cardiogenic shock.

Discussion

Intracoronary radiation therapy has been shown to be an effective treatment for decreasing neointima formation after performing coronary intervention for treating in-stent restenosis, yet its biggest pitfalls are the potential stent thrombosis and edge restenosis.[2)8)12-14)] More specifically, the rate of LST was reported to be 3-10% after brachytherapy.[2)8)14)] The prolonged use of clopidogrel has been shown to significantly reduce the rate of LST; thus, medicating with clopidogrel for at least 12 months is currently recommended for all the patients receiving brachytherapy.[6)7)] The potential mechanisms that are responsible for late thrombosis after coronary brachytherapy include impaired endothelialization, persistent fibrin deposition that leads to continuous platelet recruitment, positive arterial remodeling that produces stent malapposition and unhealed arterial dissection.[4)8)9)] However, a precise and proven explanation for the incidence, timing and mechanism of late LST is not yet available.

DESs are now rapidly replacing the use of bare-metal stents and brachytherapy due to their remarkable ability to reduce ISR. However, some disturbing reports on the occurrence of fatal stent thrombosis after DES implantation have been published,[5)15)] and the US FDA has recently released information on the adverse events, i.e., thrombosis and hypersensitivity reactions, that are related to the use of sirolimus-eluting stents.[16)] LST after DES implantation is considered to result from hypersensitivity to the stent materials, patient/lesion factors, cessation of antiplatelet drugs and delayed reendothelialization.[17)18)]

A recent meta-analyses reported there was no significant increase in the rate of stent thrombosis after DES implantation as long as the patients were maintained on both aspirin and a thienopyridine.[19)20)] However, we currently have no idea of when the risk of thrombosis disappears, and an appropriate duration of treatment with thienopyridines is required to prevent this complication.

Our report shows that thrombosis complications may arise as late as 54 months and 49 months after performing successful brachytherapy, even when treating these patients with antiplatelet agents. Therefore, clinicians should be concerned about the possibility of late LST in those patients who have undergone brachytherapy after new stent implantation. Although brachytherapy has been seldom employed for the recent treatment of in-stent restenosis, there are still a number of patients who have already undergone brachytherapy, so there are questions about the value of instituting antiplatelet therapy for these patients. Although the mechanism of LST could be different for DES and brachytherapy, our case reports suggest that we should be concerned about the possibility of LST or late LST after performing cytotoxic or cytostatic local intracoronary therapy. A study on the long-term clinical results and the data about endothelial healing is needed to ensure the safety after performing these procedures.

This study was supported by a grant of the Korea Health 21 R & D project, Ministry of Health & Welfare, Republic of Korea (00-PJ1-PG1-CH-01-0005).

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