CASE REPORT
DOI 10.4070 / kcj.2010.40.7.348

Print ISSN 1738-5520 / On-line ISSN 1738-5555

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Fatal Renal Bleeding in a Patient Treated With Aggressive Antithrombotic Therapy After Recurrent Coronary Stent Thrombosis

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ABSTRACT

Triple antiplatelet therapy has been known to be superior to the conventional dual regimen for preventing stent thrombosis after coronary stenting, and the addition of oral anticoagulation to antiplatelet therapy is also considered an option. However, the risks and benefits of a triple antiplatelet regimen plus additional oral anticoagulation must be taken into account. Here, we report a case of fatal renal bleeding in a patient treated with triple antiplatelet plus oral anticoagulant therapy for the prevention of recurrent stent thrombosis. **(Korean Circ J 2010;40:348-351)**

KEY WORDS: Drug-eluting stents; Coronary thrombosis; Drug combinations.

Introduction

Stent thrombosis is a troublesome complication of coronary stenting, and its optimal treatment still needs to be determined. Triple antiplatelet therapy has recently been reported to be superior to the conventional dual regimen for preventing stent thrombosis. The addition of oral anticoagulation to antiplatelet therapy can be considered for patients with recurrent stent thrombosis. However, the benefit of additional warfarin therapy to antiplatelet therapy has not been widely evaluated. Furthermore, potential bleeding after additional anticoagulation can result in lethal complications.

Here, we report a case of fatal renal bleeding in a patient treated with triple antiplatelet plus oral anticoagulant therapy for the prevention of recurrent stent thrombosis. The possible benefits and risks of aggressive antithrombotic strategies after percutaneous coronary intervention (PCI) are also discussed.

Received: February 18, 2010
Accepted: April 5, 2010
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Case

A 54-year-old man was admitted to our hospital in November 2008 because of flank pain lasting 2 hours. Since 1998, the patient had been treated with peritoneal dialysis for end-stage renal disease associated with polycystic kidney disease (PKD). In 2003, he underwent the first PCI, in which 2 drug-eluting stents (DES) (Taxus 3.5×16 mm and Taxus 3.5×28 mm, Boston Scientific, Natick, MA, USA) were implanted in the right coronary artery (RCA). Aspirin (100 mg once daily) and clopidogrel (75 mg once daily) were prescribed thereafter.

In July 2008, he experienced sudden chest pain. Coronary angiography revealed near total occlusion of the RCA due to stent thrombosis (Fig. 1A). A *de novo* lesion in the proximal part of the RCA was also noted. The thrombus was removed by a suction catheter and two more DESs (Cypher 3.5×28 mm and Cypher 3.5×33 mm, Cordis, Miami, FL, USA) were implanted in the RCA (Fig. 1B). Cilostazol (100 mg twice daily) was added to the dual antiplatelet regimen. In August 2008, the patient was readmitted for unstable angina. Coronary angiography showed a recurrent stent thrombosis (Fig. 1C) and the patient was treated with thrombosuction (Fig. 1D). Aspirin and clopidogrel resistance test (VeryfyNow, Accumetics Inc., San Diego, CA, USA) results were negative. Also, no evidence of other thrombophilic risk factors such as heparin-induced thrombocytopenia or patient malcompliance was found. Warfarin was added to the triple antiplatelet therapy. The prothrombin time/international normalized ratio (PT/INR) was

maintained at 2.0 to 3.0. However, the patient was readmitted for recurrent chest pain in September 2008. Coronary angiography again revealed a recurrent stent thrombosis (Fig. 1E). After repeated thrombosuction, a bare-metal stent (Vision 3.5× 23 mm, Guidant, Temecula, CA, USA) was implanted to cover the lesion (Fig. 1F).

In November 2008, the patient visited the emergency room complaining of severe left flank pain. His blood pressure was 90/60 mmHg, and laboratory tests revealed a hematocrit of 26.4% and a PT/INR of 2.7. Abdominal computed tomogra-

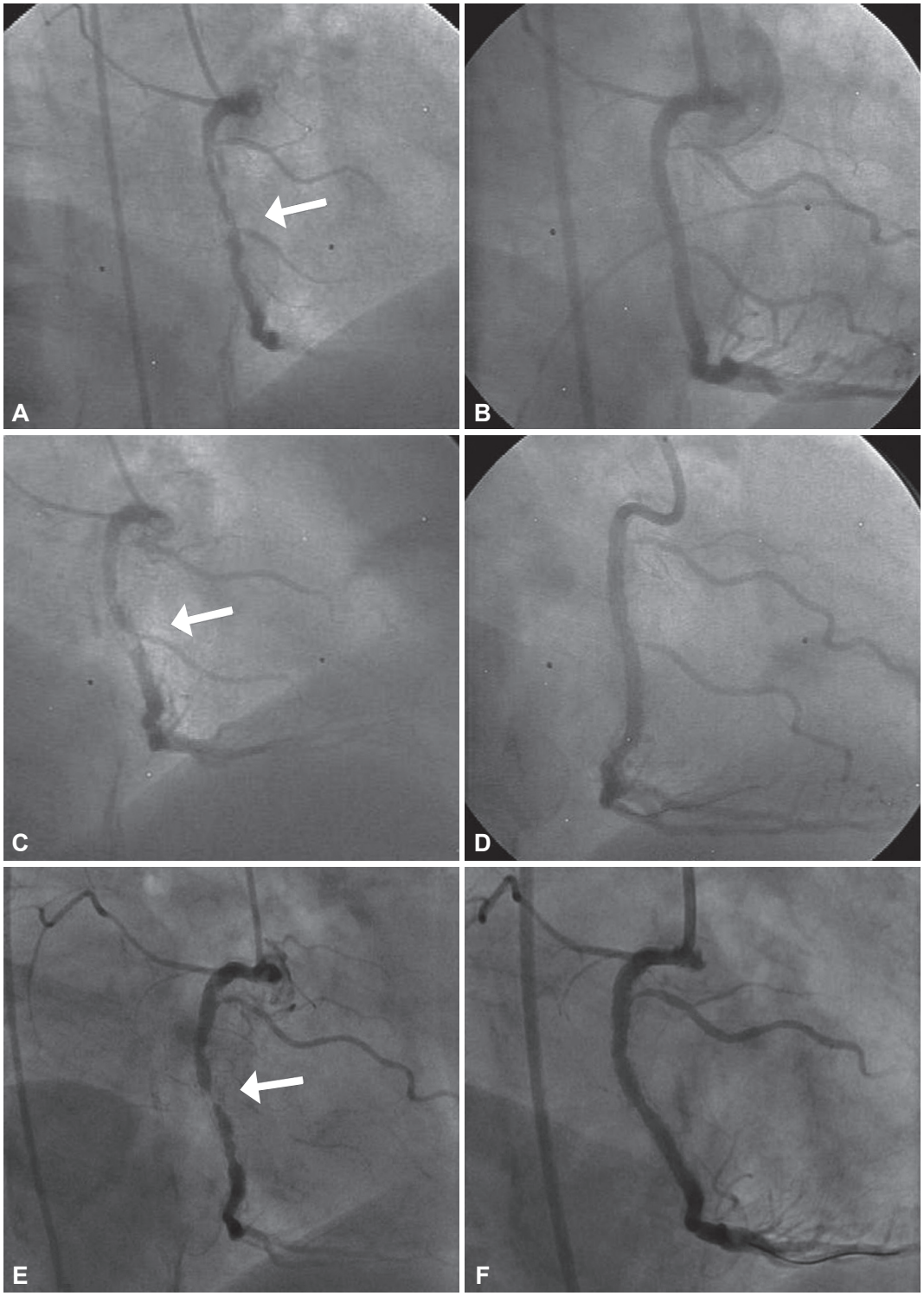

Fig. 1. Coronary angiographies taken at each event (RCA). A: stent thrombosis and partial obstruction in the RCA (arrow) in July 2008. B: RCA revascularized by thrombosuction and implantation of new stents. C: recurrent stent thrombosis and partial obstruction (arrow) in August 2008. D: lesion revascularized by thrombosuction. E: recurrent stent obstruction (arrow) in September 2008. F: lesion treated by repeated thrombosuction and new stent implantation.

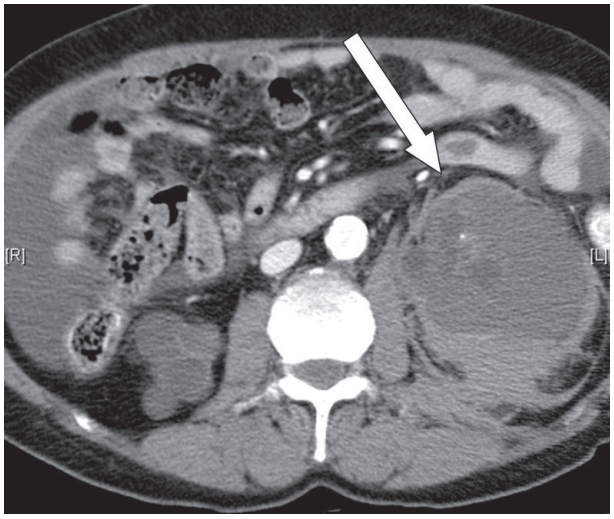

Fig. 2. Abdominal CT. Massive hemorrhage in left kidney (arrow).

phy revealed significant hemorrhage in the left kidney (Fig. 2). An urgent percutaneous embolization of the renal artery failed to stop the bleeding. Although an emergency nephrectomy was performed, disseminated intravascular coagulopathy and metabolic acidosis developed and continued unabated after surgery. On hospital day 3, the patient died of multiple organ failure.

Discussion

Stent thrombosis is a troublesome complication of PCI. It is often disastrous and is associated with high mortality rates ranging from 20% to 25%.[1] In addition, an effective and appropriate strategy for managing stent thrombosis has not been firmly established.

Premature discontinuation of dual antiplatelet therapy is a well-known cause of stent thrombosis. However, the occurrence of stent thrombosis despite adherence to the drug regimen suggests that some patients are unresponsive to clopidogrel therapy. Unresponsiveness is essentially caused by functional and genetic variations in cytochrome P450 enzymes.[2] In addition, chronic kidney disease, diabetes mellitus, reduced ventricular systolic function, acute coronary syndrome, impaired flow restoration, total occlusions, long stent length, and a number of treated lesions are reported as predictors for stent thrombosis.[3-5] Our patient had several risk factors for stent thrombosis, including end-stage renal disease and long lesion length, whereas he was not resistant to aspirin or clopidogrel, and had good compliance with antiplatelet agents.

Triple antiplatelet therapy was prescribed for our patient. In previous studies, triple antiplatelet therapy was shown to be more effective after PCI for preventing stent thrombosis or major cardiovascular events than dual antiplatelet therapy.[6-11] Currently, it is not clear whether triple therapy induces bleeding more frequently than dual therapy.[12] For recurrent stent thrombosis, oral anticoagulation can be considered as an option,[13][14] although there is controversy regarding the value of warfarin administration after PCI. When oral anticoagulation is considered in patients with stent thrombosis, the risk of bleeding is a major concern.[13][15] One recent study reported that anticoagulant therapy did not increase the risk of major bleeding in patients with atrial fibrillation undergoing PCI.[15] However, some studies suggest that warfarin increases the risk of major bleeding when added to antiplatelet therapy.[5] Although warfarin in combination with antiplatelet therapy may be an option for treating stent thrombosis, oral anticoagulation for the prevention of stent thrombosis needs to be individualized. Particularly, the bleeding risk of each patient should be carefully assessed before treatment.

Our patient suffered from massive renal hemorrhage that resulted in death. He had risk factors for bleeding such as end-stage renal disease and concomitant triple antiplatelet therapy plus oral anticoagulation.[4][5] Moreover, PKD is known as a cause of recurrent hematuria and renal hemorrhage.[16] Because renal cysts are prone to rupture after even light trauma, a polycystic kidney can be a major source of bleeding.

A thorough evaluation of the bleeding risks of PKD before the implementation of aggressive antithrombotic therapy could have been helpful in our patient. Major bleeding can be disastrous in coronary artery disease patients for several reasons. Heart function is decreased in many coronary artery disease patients and patients are more likely to have comorbidities such as hypertension, diabetes, and renal insufficiency. Compensatory elevation of heart rate in response to hypovolemia can be masked in patients who are taking beta blockers. As a result, early detection of bleeding can be difficult. Therefore, every effort should be made to detect any symptoms or signs of bleeding in these patients.

In conclusion, although aggressive antithrombotic therapy can be considered an option for treatment of recurrent stent thrombosis, the patient's risk of bleeding should be evaluated thoroughly. The risks and benefits of triple antiplatelet therapy plus additional oral anticoagulation must be taken into account.

REFERENCES

1) Honda Y, Fitzgerald PJ. *Stent thrombosis: an issue revisited in a changing world. Circulation 2003;108:2-5.*
2) Gurbel PA, DiChiara J, Tantry US. *Antiplatelet therapy after implantation of drug-eluting stents: duration, resistance, alternatives, and management of surgical patients. Am J Cardiol 2007;100:18M-25M.*
3) Jaffe R, Strauss BH. *Late and very late thrombosis of drug-eluting stents: evolving concepts and perspectives. J Am Coll Cardiol 2007;50:119-27.*
4) Manzano-Fernandez S, Marin F, Pastor-Perez FJ, et al. *Impact of chronic kidney disease on major bleeding complications and mortality in patients with indication for oral anticoagulation undergoing coronary stenting. Chest 2009;135:983-90.*
5) Manzano-Fernandez S, Pastor FJ, Marin F, et al. *Increased major bleeding complications related to triple antithrombotic therapy usage in patients with atrial fibrillation undergoing percutaneous coronary*

artery stenting. Chest 2008;134:559-67.

6) Jeong YH, Lee SW, Choi BR, et al. *Randomized comparison of adjunctive cilostazol versus high maintenance dose clopidogrel in patients with high post-treatment platelet reactivity: results of the ACCEL-RESISTANCE (Adjunctive Cilostazol Versus High Maintenance Dose Clopidogrel in Patients With Clopidogrel Resistance) randomized study. J Am Coll Cardiol 2009;53:1101-9.*
7) Han Y, Li Y, Wang S, et al. *Cilostazol in addition to aspirin and clopidogrel improves long-term outcomes after percutaneous coronary intervention in patients with acute coronary syndromes: a randomized, controlled study. Am Heart J 2009;157:733-9.*
8) Lee SW, Park SW, Kim YH, et al. *Drug-eluting stenting followed by cilostazol treatment reduces late restenosis in patients with diabetes mellitus the DECLARE-DIABETES Trial (A Randomized Comparison of Triple Antiplatelet Therapy with Dual Antiplatelet Therapy After Drug-Eluting Stent Implantation in Diabetic Patients). J Am Coll Cardiol 2008;51:1181-7.*
9) Lee SW, Park SW, Kim YH, et al. *Comparison of triple versus dual antiplatelet therapy after drug-eluting stent implantation (from the DECLARE-Long trial). Am J Cardiol 2007;100:1103-8.*
10) Jeon DS, Yoo KD, Park CS, et al. *The effect of cilostazol on stent thrombosis after drug-eluting stent implantation. Korean Circ J 2010;40:10-5.*
11) Yang TH, Kim DI, Kim JY, et al. *Comparison of triple anti-platelet therapy (aspirin, clopidogrel, and cilostazol) and double anti-platelet therapy (aspirin and clopidogrel) on platelet aggregation in type 2 diabetic patients undergoing drug-eluting stent implantation. Korean Circ J 2009;39:462-6.*
12) Francescone S, Halperin JL. *"Triple therapy" or triple threat?: balancing the risks of antithrombotic therapy for patients with atrial fibrillation and coronary stents. J Am Coll Cardiol 2008;51:826-7.*
13) Rossini R, Musumeci G, Lettieri C, et al. *Long-term outcomes in patients undergoing coronary stenting on dual oral antiplatelet treatment requiring oral anticoagulant therapy. Am J Cardiol 2008;102:1618-23.*
14) Ruiz-Nodar JM, Marin F, Hurtado JA, et al. *Anticoagulant and antiplatelet therapy use in 426 patients with atrial fibrillation undergoing percutaneous coronary intervention and stent implantation implications for bleeding risk and prognosis. J Am Coll Cardiol 2008;51:818-25.*
15) Lip GY, Karpha M. *Anticoagulant and antiplatelet therapy use in patients with atrial fibrillation undergoing percutaneous coronary intervention: the need for consensus and a management guideline. Chest 2006;130:1823-7.*
16) Grantham JJ. *Clinical practice: autosomal dominant polycystic kidney disease. N Engl J Med 2008;359:1477-85.*