



Formation of and countermeasures for subacute coronary stent thrombosis in elderly diabetic patients

Z.-F. Li¹, Y.-P. Zhang², Z.-Q. Qin², X.-L. Li¹, C.-H. Gao¹, S. Yang¹ and Z.-J. Chen¹

¹Department of Cardiology, Yongchuang Hospital, Chongqing Medical University, Chongqing, China

²Department of Cardiology, People's Hospital of Tongliang County, Chongqing, China

Corresponding author: Y.-P. Zhang
E-mail: lzf56888@163.com

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ABSTRACT. The aim of this study was to evaluate and investigate the pathogenetic mechanism and countermeasures of subacute thrombosis (SAT) after coronary stenting in elderly diabetic patients. The clinical characteristics and pathogenetic mechanisms in 3 cases of SAT after stent implantations in elderly diabetic patients were retrospectively examined to determine the treatment strategies for SAT. Among 98 patients with diabetes who had coronary stents implanted or were >60 years of age, three (3.06%) had SAT. One case of SAT was diagnosed by angiography; coronary balloon dilatation, thrombolysis, and reperfusion resulted in full recovery in this case. The second case involved potential SAT, and in the third case, SAT was not ruled out. Two cases were characteristic of ST-segment elevation myocardial infarction, and one case, in which SAT was not ruled out, resulted in sudden death. SAT within a stent may be related to intraoperative stent

malapposition caused by a grade C lesion, age, diabetes, chronic total occlusion, or postoperative irregular administration of medication.

Key words: Elderly diabetes; Coronary stent; Thrombosis

INTRODUCTION

Stent thrombosis (ST) is serious complication of coronary intervention treatment that has an incidence of only 0.9-1% but a poor prognosis (Trabattoni et al., 2007). The higher incidence of subacute thrombosis (SAT) with increase in age, hypertension, and diabetes could lead to the deaths of one-third to one-half of the affected patients. According to stent implantation time, ST was divided into acute (<24 h), subacute (1-30 days), end stage (1-12 months), and very end stage (>1 year) thrombosis (Moussa et al., 1997; Farb et al., 2003). The incidence of SAT in patients with ST is approximately 50% (Trabattoni et al., 2007). SAT after percutaneous coronary intervention (PCI) occurs mainly as follows: 1) Independent factors for SAT include diabetes, renal insufficiency, acute coronary syndrome, ST-segment elevation myocardial infarction, long lesions, and left anterior descending branch (de la Torre-Hernández et al., 2008). 2) Stent factors: incomplete stent expansion, incomplete stent coverage of a lesion, residual stenosis, and residual dissection after stenting all cause thrombosis. Metal stents promote thrombosis formation. Drug-coated stents may inhibit endometrial hyperplasia and reduce the restenosis rate; however, endothelialization may be delayed. The compatibility and endothelial incomplete repair of the stents may also induce blood hypercoagulability. These factors could all lead to an increased risk of thrombosis (Harper, 2007). 3) Anticoagulant therapy: anticoagulant drug discontinuation or resistance to clopidogrel hydrogen and aspirin (Nguyen et al., 2005). 4) Intraoperative operating factors: guidance of a steel wire through intraoperative PCI, balloon dilatation, and stent release could all damage blood vessels, leading to endometrial tearing, which could cause exposure to subendometrial collagenous fibers, activate the coagulation system, and then lead to thrombus formation (Neumann et al., 1996). The diameter of the target blood vessel and the degree of residual stenosis are also important factors affecting stent thrombosis. Some studies found that incomplete stent expansion was an independent risk factor of postoperative stent thrombosis (Cheneau et al., 2003). Ischemia reperfusion injury mechanisms might also be involved in stent thrombosis.

The purpose of this study was to evaluate and investigate the pathogenetic mechanism of and countermeasures for subacute thrombosis in elderly patients with diabetes combined with coronary diseases. Advanced age, diabetes, chronic total occlusion (CTO), diffuse calcification, bifurcation lesions, and anticoagulant treatment discontinuation were pathogenetic mechanisms of subacute thrombosis, providing references for the preventive treatment of subacute stent thrombosis after PCI.

The clinical characteristics and treatment of three patients with SAT after undergoing stenting from October 2010 to August 2011 in our department were reported as follows.

MATERIAL AND METHODS

General data

From October 2010 to August 2011, 98 patients aged >60 years (with or without dia-

betes) underwent PCI in our department, three of whom (two men and one woman) had SAT in the coronary stent. These patients were aged 61-82 years (mean age, 73.3 years), as shown in Table 1.

Table 1. General clinical data of three patients with coronary stent subacute thrombosis.

Items	Case 1	Case 2	Case 3
Age (years)	61	78	82
Hypertension	Yes	Yes	No
Diabetes	Yes	Yes	Yes
CTO	Yes	No	Yes
Diagnosis	Old MI	UAP	Old MI
Left ventricular ejection fraction	54	42	50

CTO = chronic total occlusion; MI = myocardial infarction; UAP = unstable angina pectoris.

PCI treatment

The three patients underwent elective operation and were administered preoperative 100 mg/day aspirin and 75 mg/day clopidogrel for more than 1 month. All of the patients had multivessel disease that had nine target lesion parts and was classified as grade C lesions according to the American College of Cardiology and American Heart Association. Two patients had CTO: nine drug-eluting stents (DES) were implanted, without postoperative residual stenosis, with forward flow to thrombolysis in myocardial infarction (TIMI) grade 3. Three patients underwent full pre-dilatation before stenting, and two patients underwent post-dilatation after stenting. Because of the tortuous and calcified lesions, a high-pressure balloon of the same size as the stent was used. Postoperative stent inflation was good, without residual stenosis, as shown in Table 2.

Table 2. Coronary artery lesions and PCI treatment materials of three patients with coronary stent SAT.

Items	Case 1	Case 2	Case 3
PCI pathogenesis (days)	70	30	84
Pathological vessels	3	2	3
Stent-implanted parts	LAD middle and distal part, LCX proximal part, RCA middle part	LAD middle part, RCA middle part	LM middle part, LAD middle and distal part, LCX middle part
Lesion characteristics	Calcified diffuse CTO	Calcified tortuous	Calcified diffuse CTO
Longest lesions (mm)	38	18	20
SAT vessel	LAD	LAD	LCX
SAT stent diameter (mm)	2.75	3.0	2.5
SAT stent length (mm)	24	24	18
Post-dilatation	Yes	Yes	Yes
Malapposition	No	No	No
Preoperative TIMI flow	0	3	0
Postoperative TIMI flow	3	3	3

PCI = percutaneous coronary intervention; SAT = subacute thrombosis; TIMI = thrombolysis in myocardial infarction; LAD = left anterior descending artery; LCX = left circumflex artery; RCA = right coronary artery; CTO = chronic total occlusion; LM = left main coronary artery.

RESULTS

Postoperative symptoms occurred in three patients for 2-10 days. In case 1, continu-

ous 3.0 x 21 and 2.75 x 24 mm DES in the middle and distal part of the left anterior descending (LAD) artery, 3.0 x 18 mm DES in the left circumflex (LCX) artery, and 3.0 x 15 mm DES in the right coronary artery were implanted. On postoperative day 6, there was no angina, cardiac function was class I, and the clinical manifestation was very stable. On postoperative day 7, the patient experienced sudden death after a cold. In case 2, 3.0 x 24 and 3.0 x 28 mm DES were implanted in the LAD and LCX. Postoperative angina was terminated. At 6 days postoperatively, the patient self-discontinued the aspirin and clopidogrel. On postoperative day 10, the patient experienced myocardial infarction; after 10 h, he was diagnosed with acute myocardial infarction in our department. Anterior descending stent thrombosis was observed on coronary angiography, with forward flow to TIMI grade 0. Immediate and repeated stent percutaneous transluminal coronary angioplasty (PTCA) was performed, and 200,000 U coronary urokinase was injected. Residual stenosis was not seen on coronary angiography, and the forward flow was recovered to TIMI grade 3.

In case 3, a 3.0 x 24 mm DES was implanted in the LAD, a 3.5 x 15 mm DES was implanted in the left main, and a 2.5 x 18 mm DES was implanted in the LCX artery. On postoperative day 5, the patient experienced chest pain for >20 min; II, III, aVF, and ST-segment elevation was >0.1 mm; and CK-MB was increased significantly to more than twice the normal value. The patient was diagnosed with acute inferior diaphragmatic infarction. Because the chest pain was relieved after approximately 30 min without abnormal vital signs and because the patient was very elderly and his family members refused coronary angiography, PTCA, and thrombolysis, conservative treatment was performed. After 2 weeks, the patient's condition improved and he was discharged. ST treatments and results are shown in Table 3.

Table 3. Treatments and results of 3 patients with coronary stent SAT.

Items	Case 1	Case 2	Case 3
SAT occurrence time (days)	7	10	3
SAT symptom	Sudden death	AMI	AMI
Coronary angiogram	No	Yes	No
PCI treatment	No	Yes	No
Clinical results	Sudden death	Improved	Improved

SAT = subacute thrombosis; PCI = percutaneous coronary intervention; AMI = acute myocardial infarction.

DISCUSSION

ST is a serious complication of coronary intervention treatment and often endangers patients' lives. The mechanism underlying ST involves multiple factors, so prevention is not very effective. As reported in the literature (Moussa et al., 1999; Cheneau et al., 2003; Buonamici et al., 2007; Machecourt et al., 2007), ST formation is related to many factors such as acute coronary syndrome, plaque rupture, platelet activation, and increased agglutinant release *in vivo*. In some cases, aspirin and clopidogrel were not fully used and were even discontinued (case 2 in this paper). Other factors are agedness, diabetes, and chronic renal insufficiency. The DES effectively reduces the rate of stent restenosis and major adverse cardiac events of the target lesion (or target vessel) revascularization by inhibiting endometrial hyperplasia. However, the ST incidence of DES, especially SAT, remains a concern. The ESTROFA registry in Spain (de la Torre-Hernández et al., 2008) showed that the incidence of ST is 1.2% and that 50% of these cases involved SAT. DES was used in three cases of SAT in the present study.

The Academic Research Consortium (ARC) (Cutlip et al., 2007), consisting of data from the United States and Europe in 2007, divided ST into the following three categories. The first is definite or confirmed ST: acute coronary syndrome, definite radiographic findings of ST, or thrombosis in a stent within 5 mm of the proximal or distal portion confirmed by autopsy. The second is probable ST: any unexplained death within 30 days; postoperative myocardial infarction related to definite myocardial ischemia in the coronary region supplied by the implanted stent, without other obvious reasons and without imaging findings to confirm stent thrombosis. The third is possible ST: any unexplained death within 30 days. Case 2 in this paper involved definite SAT with a definite reason for discontinuation of clopidogrel, aspirin, or some other antiplatelet agent. The ARC believes that SAT had a direct relationship with stent malapposition, residual dissection, or failure of a stent to completely cover a lesion. Cases 1 and 3 in this article involved occlusive diseases, making it difficult to avoid residual dissection. Extensively calcified and tortuous vessels caused by advanced age and diabetes, and the small target vessels were all factors for stent malapposition. Although all such lesions were treated with full pre- and post-dilatation, it was difficult to avoid individual stent malapposition. Compared with patients who have coronary disease and normal sugar metabolism, these types of patients are susceptible to SAT because of a large number of lesions and implanted stents (Schühlen et al., 1998; Buonamici et al., 2007). Because of diffuse lesions in the vessels of patients with diabetes, the pre-expanded balloon had a smaller maximum diameter and the implanted stent had a longer length and smaller diameter during PCI (Goraya et al., 2002). These might be causes of the high SAT incidence in patients with advanced age or diabetes.

Analysis of the above three cases of SAT highlighted the following results: 1) antiplatelet therapy should be strictly regulated; 2) in high-risk elderly patients who have diabetes, CTO, or diffusely calcified or bifurcated lesions, PCI or coronary artery bypass grafting should be performed after assessing SYNTAX score and radiography results (Sianos et al., 2005; Ong et al., 2006); and 3) immediate and decisive PCI treatment should be provided for patients with SAT.

Conflicts of interest

The authors declare no conflict of interest.

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