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Case Report

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Very Late Bare Metal Stent Thrombosis: What Can Be The Role of Instent Re-stenosis and Hyperhomocysteinemia?

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ABSTRACT

A 62-years old man was admitted to emergency department suffering from chest pain. Resting ECG revealed ST elevation on inferior leads and he was diagnosed with acute inferior myocardial infarction. His past medical history revealed that a bare metal stent had been implanted in his circumflex coronary artery upon stable angina pectoris 45 months ago. Immediately performed coronary angiography demonstrated the occlusion of the stent in the circumflex coronary artery. A new bare metal stent was implanted and TIMI 3 flow was established after initial balloon angioplasty. No other causes but vitamin B12 deficiency and hyperhomocysteinemia were found for this non-smoker patient among other laboratory tests.

Keywords: *Stent, Thrombosis, Myocardial infarction*

ÖZET

Çok Geç Dönem Çıplak Metal Stent Trombozu: Stent İçi Restenozun ve Hiperhomosisteineminin Rolü Ne Olabilir?

Altmışiki yaşındaki erkek acil servise göğüs ağrısı şikayeti ile kabul edildi. İstirahat elektrokardiyografisinde inferior derivasyonlarda ST yükselmesi saptaması üzerine hastaya akut inferior miyokard infarktüsü tanısı konuldu. Hastadan edinilen tıbbi hikaye doğrultusunda 45 ay öncesinde başka bir merkezde kararlı angina pektoris kliniği ile sirkumfleks koroner arterine çıplak metal stent takıldığı öğrenildi. Acil yapılan koroner anjiografisinde sirkumfleks arterdeki önceki stentin akut oklüzyonu saptandı. Balon anjioplasti ardından yeni bir çıplak metal stent implante edilerek sirkumfleks arterde TIMI-3 akım elde edildi. Sigara kullanmadığı bilinen hastada tromboz etyolojisini saptamak amaçlı yapılan testler sonucunda vitamin B12 eksikliği ve hiperhomosisteinemi saptandı.

Anahtar Kelimeler: *Stent, Tromboz, Miyokard infarktüsü*

Stent thrombosis (ST) is defined as an abrupt onset of cardiac symptoms along with an elevation in levels of biomarkers or electrocardiographic evidence of myocardial injury after stent deployment. Although late drug eluting ST is often seen due to early discontinuation of clopidogrel treatment especially in diabetic patients, late bare metal ST is seen exclusively in cases with intracoronary radiation therapy. Moreover, late thrombosis beyond one year of implantation of bare metal stents is quite unusual (1). We present a case of very late acute bare metal stent thrombosis (VLST) in a middle-aged man. We suggest hyperhomocysteinemia and in-stent restenosis as the possible causes of ST in the present case.

CASE REPORT

A 58-years old, non-diabetic, hypertensive man was admitted to out-patient cardiology clinic with typical chest pain occurring at physical activity in May 2005. Treadmill test revealed ECG changes suggestive of ischemia and coronary angiography was performed. 80 % critical stenosis was detected in his circumflex coronary artery (Figure 1) and a 3 x 14-mm bare metal stent was implanted at 14 atm without balloon predilatation (Figure 2). One day later, patient was discharged with indefinite aspirin and one month of clopidogrel treatment. Statin and ACE- inhibitory therapy were also prescribed. 45 months passed without any medical event.

While on aspirin therapy, patient was admitted to emergency unit suffering from chest pain of two hours duration in February 2009. ECG revealed acute inferior myocardial infarction. Immediately performed coronary angiography showed occlusion of previously implanted circumflex stent (Figure 3). After insertion of coronary guidewire, there was no flow restoration. Thromboaspiration was not performed due to technical reasons. Balloon angioplasty was performed with

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2x12-mm balloon (Figure 4). Although the patient was a candidate for surgery due to ostial left anterior descending coronary artery lesion, a 3x28-mm bare metal stent was implanted with restoration of TIMI-3 flow (Figure 5) because of unsuccessful previous balloon angioplasty and ongoing chest pain. At the day 3, the peaks of CK and CK-MB enzymes were observed. Transthoracic echocardiography showed little impairment of left ventricular systolic function with global EF 45 %. Routine blood biochemistry and hemograms tests were performed after 12-hour overnight fast. Glucose, cholesterol and hematocrit levels were within normal limits while vitamin B12 level was 153.9 pg/ml (191 pg/ml – 663 pg/ml). Because of low vitamin B12 level, another blood sample was taken in the following morning after 12-hour overnight fast and homocysteine, protein C, protein S, and lipoprotein (a) levels were measured. Only homocysteine level was abnormally high at 29.3 micromol/L which was two-fold of the upper limit for that age. The patient was supplemented with folic acid for hyperhomocycteinemia. Patient was sent to surgery after a month of aspirin and clopidogrel treatment.

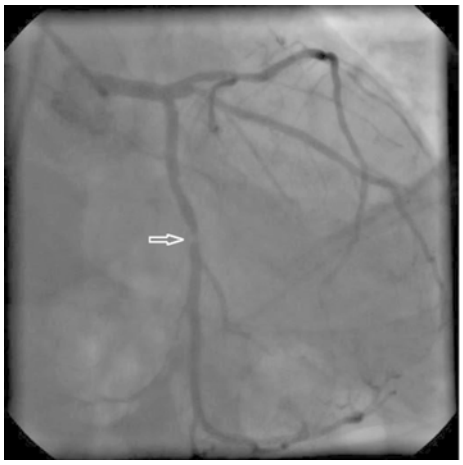

Figure 1. *Shows 80 % stenosis (arrow) in circumflex artery.*

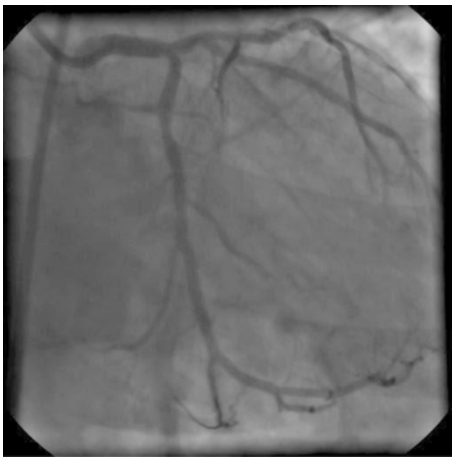

Figure 2. *Shows angiographic result after 3x14 mm BMS implantation.*

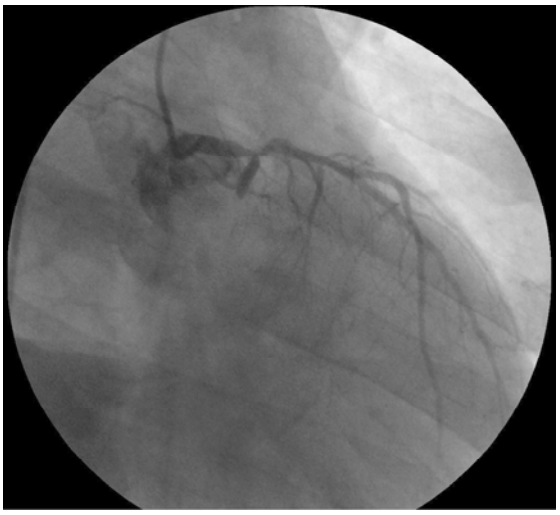

Figure 3. *Shows acute stent thrombosis after 45 months.*

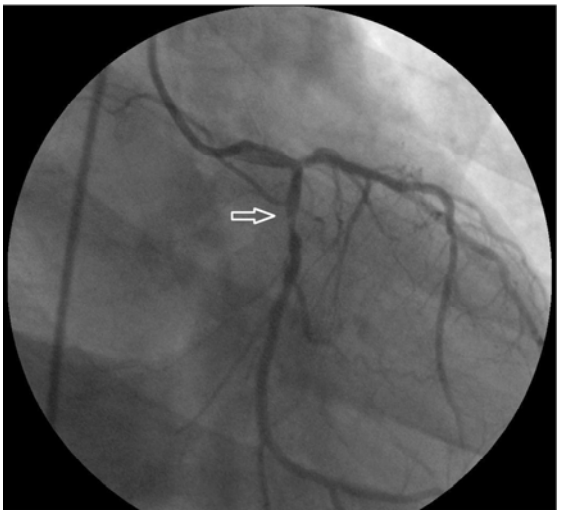

Figure 4. *Shows resudial thrombus (arrow) after balloon predilatation.*

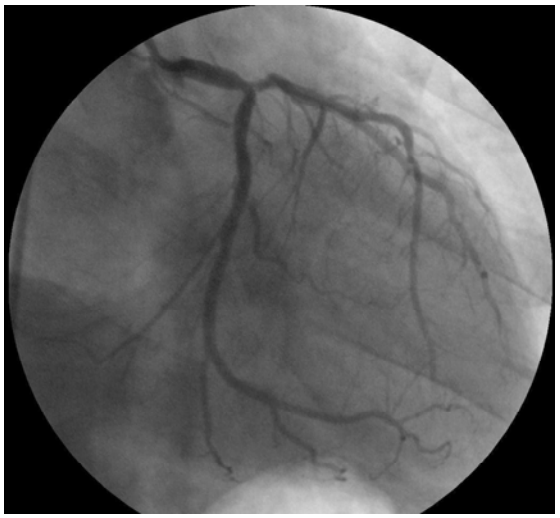

Figure 5. *Shows good angiographic result after 3x28 mm BMS implantation.*

DISCUSSION

Most recently accepted definition established by the Academic Research Consortium classifies ST as: early (occurring within 30 days), late (30 days to one year) or very late (after one year) (1). A 30-day incidence of ST of 0.9 % and most events occur within one week. The incidence of ST is associated with a high frequency of major adverse clinical consequences. There may be multiple causes for early stent thrombosis (2). Stent underexpansion, incomplete apposition, dissection, thrombus, tissue protrusion, persistent slow flow, acute coronary syndrome, vessel size/lesion length and left ventricular function are some of the suggested causes in medical literature. The Armed Forces Institute of Pathology has reported an autopsy study declaring bifurcation lesion, radiation therapy, treatment of diffuse instent re-stenosis with another stent, disruption of vulnerable plaque near stent and stent strut penetration of necrotic core as the risk factors for thrombosis (3).

Although drug eluting stent thrombosis is more often seen due to early discontinuation of clopidogrel treatment especially in diabetic patients, late bare metal stent thrombosis is almost exclusively associated with intracoronary radiation therapy. Although some case reports are available describing VLST without any established causes (4), there is no randomised trial declaring true incidence of VLST of bare metal stent in literature. In a case report by Bertrand et al. (5), instent re-stenosis after 5 years of initial stent implantation has been linked to VLST. In their case report, Trabattoni and Bartorelli proposed instent re-stenosis as the main mechanism leading to abrupt thrombotic vessel closure and acute myocardial infarction (6). Danenberg et al. (7) found that acute myocardial infarction could be the late presentation of intracoronary stent implantation and proposed strenuous exercise as a possible cause. Celik et al. (8). suggested an association between ST and exercise-induced hypercoagulable state.

In our case, we did not observe much thrombus burden, distal embolization or no-reflow after balloon angioplasty. This finding suggested us that in-stent critical stenosis would have been the main mechanism. Our patient presented with acute myocardial infarction. In their article, Chen and et al. (9) discovered that more than one third of bare metal instent re-stenosis episodes present with myocardial infarction or unstable angina requiring hospitalization. In their retrospective analysis, Nayak et al. (10) concluded that myocardial infarction could be the presentation of instent re-stenosis.

Although exercise was not an issue, hypercoagulable state was proved by hyperhomocysteinemia in our patient. A large number of studies supported the presence of an association between elevated homocysteine levels and various atherothrombotic disease including stoke, venous thromboembolism and ischemic cardiac disease (11). Histopathologic hallmarks of atherothrombosis related to elevated homocysteine levels include intimal thickening, elastic lamina disruption, smooth muscle hypertrophy, platelet accumulation, and the formation of platelet-enriched occlusive thrombi (12). Several studies have demonstrated the involvement of homocysteine in the process of in-stent restenosis (13). Our patient did not have any illnesses affecting homocysteine metabolism as gastritis, anemia, chronic kidney disease, hypothyroidism, alcoholism, psoriasis, current smoking, known cancer or medication but only had deficiency of vitamin B12 as the possible causes of hyperhomocysteinemia. Several randomized clinical trials are underway to address the effect of folate, vitamin B_6, and vitamin B_{12} supplementation on cardiovascular disease. Until complete results of these studies become available, screening for hyperhomocystinemia in patients undergoing coronary stenting is only recommended in the case of premature atherosclerotic disease (patients <45 years of age), when there is a paucity of more conventional risk factors, and in patients with a history of unexplained venous thrombosis.

Stent underexpansion, distal poor run-off, or stent fracture may effect the long-term patency of stents. Initial use of IVUS during stent deployment showed that 80% of stents were underexpanded and led to the hypothesis that ST might be decreased as a result of optimal stent placement under IVUS guidance. We did not perform IVUS or angioscopic study before coronary angioplasty in this case, so we do not know the exact mechanism of ST. When considering minimal thrombus burden, absence of distal embolization and absence of no-reflow, high degree instent re-stenotic lesion seems logical as the main mechanism. When we studied on previous angioplasty records, we found that 3-mm stent diameter was appropriate for the patient and the stent expanded well without any residual stenosis. Last angioplasty records also showed that there was not any new atherosclerotic lesion in the vessel stented and this finding makes the distal poor run-off unlikely for cause of stent thrombosis. Also, we do not think that 14-mm long stent may fracture easily in the mid-portion of the circumflex artery.

In conclusion, high turbulent flow and shear stress associated with possible instent re-stenotic lesion and augmented procoagulant state associated with hyperhomocysteinemia may be the causes of very late bare metal stent thrombosis in our patient. Optimization of stent deployment, anti-coagulation therapy, and screening for hyperhomocystinemia in young patients undergoing coronary stenting can help in preventing late ST.

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