A case of late stent thrombosis after paclitaxel-eluting stent implantation

Paklitaksel salınımlı stent uygulaması sonrasında geç stent trombozu: Olgu sunumu

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Drug-eluting stents are widely used in the treatment of coronary artery disease, but late stent thrombosis is still a concern. A 54-year-old male patient who presented with unstable angina pectoris underwent paclitaxel-eluting stent implantation for 90% stenosis in the right coronary artery (RCA). He was asymptomatic during follow-up and clopidogrel was discontinued 13 months after the procedure. However, 17 months after stent implantation he presented with acute inferior myocardial infarction. Coronary angiography revealed total in-stent thrombosis in the RCA. Thrombotic occlusion was easily passed with a floppy guide wire and balloon angioplasty was successful resulting in TIMI II-III flow. The patient was asymptomatic during hospital stay and was discharged on appropriate medications.

Key words: Coronary disease; coronary thrombosis/etiology; paclitaxel; stents/adverse effects.

İlaç salınımlı stentler koroner arter hastalığının tedavisinde yaygın olarak kullanılmaktadır; ancak, geç dönem stent trombozu halen sorun olmayı sürdürmektedir. Kararsız angina pektoris tablosuyla başvuran 54 yaşındaki bir erkek hastaya, sağ koroner arterde %90 darlık görülmesi üzerine paklitaksel salınımlı stent takıldı. Takip dönemini asemptomatik geçiren hastada, stent takılmasından 13 ay sonra klopidogrel kullanımına son verildi. Ancak, işlemden 17 ay sonra hasta akut inferior miyokard infarktüsüyle tekrar başvurdu. Koroner anjiyografide sağ koroner arterde tam stent trombozu görüldü. Trombotik tıkanıklık kılavuz telle geçildikten sonra balon anjiyoplasti yapıldı ve TIMI II-III akım elde edildi. Hastanedeki takibinde asemptomatik olan hasta uygun ilaçlarla taburcu edildi.

Anahtar sözcükler: Koroner hastalık; koroner tromboz/etyoloji; paklitaksel; stent/yan etki.

Drug-eluting stents are widely used in the treatment of coronary artery disease. While the problem of in-stent restenosis is mostly overcome in these stents, late stent thrombosis is still a concern.

We report a case of late stent thrombosis seen 17 months after paclitaxel-eluting stent implantation.

CASE REPORT

A 54-year-old male smoker who was previously asymptomatic presented with unstable angina pectoris. Coronary angiography revealed 90% stenosis in the right coronary artery (RCA), and insignificant stenoses in the left anterior descending and circumflex coronary arteries (Fig. 1a). A paclitaxel-eluting stent 2.5x16 mm in size (Taxus, Boston Scientific, Natick, Massachusetts, USA) was implanted in the RCA in August 2004. The patient was discharged without complication on atorvastatin 20 mg/day, aspirin 300 mg/day, and clopidogrel 75 mg/day. He was asymptomatic during follow-up and clopidogrel was discontinued 13 months after the procedure. In October 2005, he presented to the emergency department with acute inferior myocardial infarction. Following intravenous bolus tirofiban administration, the patient was taken to the catheterization laboratory for emergent percutaneous coronary intervention (PCI). Coronary angiography revealed total in-stent thrombosis in the RCA (Fig. 1b). Thrombotic occlusion was easily passed with a floppy guide wire and balloon angioplasty was successful resulting in TIMI II-III flow and dissipation of the thrombus (Fig. 1c, d). Tirofiban infusion was continued for 24 hours. The patient was asymptomatic

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at clinical follow-up and was discharged on atorvastatin 20 mg/day, aspirin 300 mg/day, clopidogrel 75 mg/day, and ramipril 2.5 mg/day.

DISCUSSION

Smooth muscle cell proliferation and migration after vessel injury associated with bare metal stents play an important role in the pathogenesis of in-stent restenosis. A neointimal layer of extracellular matrix and collagen forms, which may impinge on the vessel lumen. Paclitaxel inhibits vascular smooth-muscle-cell proliferation and reduces neointimal mass. Local delivery of paclitaxel through a coronary stent has been shown to reduce restenosis rates and percent diameter stenosis and to provide other angiographic benefits compared with bare-metal stents.[1] Previously, late thrombotic occlusions of Taxus stents were reported, with late occurrence after six months suggesting a thrombotic genesis.[2,3] Premature discontinuation of antiplatelet therapy and antiplatelet monotherapy were shown to be predictors of late stent thrombosis.[4,5] Delayed endothelialization of stent struts was reported to cause late stent thromboses.[6] Polymers used in drug-eluting stents may cause late stent thrombosis, as well.[7]

The lowest rate for stent thrombosis was reported to be around 0.4% and it raised to 2.8% in multivessel stenting. Stent thrombosis at one year was found in 0.4% of cases with sirolimus-eluting stents, being 0.6% with polymer-based paclitaxel-eluting stents at nine months.[8-10] In another study, angiographic late stent thrombosis at 18 months was reported to be 0.35% in about 2000 patients.[11] A meta-analysis of 11 randomized studies including around 5,000 patients showed no evidence that either sirolimus- or paclitaxel-eluting stents had higher stent thrombosis

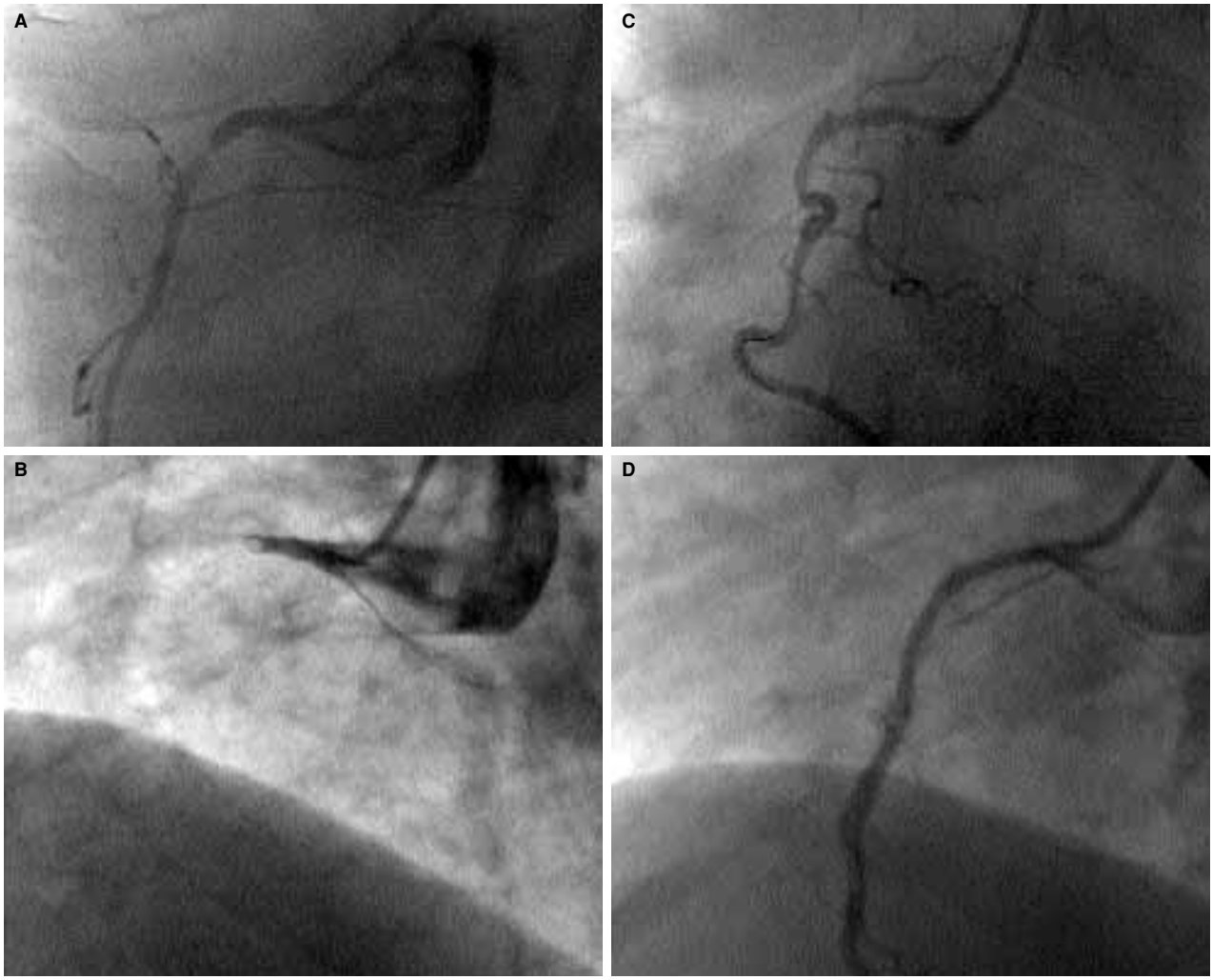

Figure 1. (A) Stenosis in the right coronary artery (RCA) on first presentation. **(B)** Total in-stent thrombosis in the proximal right coronary artery (RCA). **(C)** Thrombotic occlusion of the RCA was recanalized with simple balloon angioplasty. **(D)** TIMI II-III flow in the RCA after balloon angioplasty.

rates than bare metal stents.[12] In another study comparing sirolimus- and paclitaxel-eluting stents, no difference was observed with regard to stent thrombosis rates.[13]

Clinical characteristics such as age, diabetes, low ejection fraction, chronic renal failure, acute coronary syndrome, and bifurcation lesions are associated with increased stent thrombosis.[4] Postprocedural small lumen size, residual dissection, multiple stenting, unprotected left main stenting, and previous brachytherapy increase stent thrombosis.[14-16] Acetylsalicylic acid and clopidogrel resistances also contribute to stent thrombosis.[17,18] The most important predisposing factor for stent thrombosis is cessation of antithrombotic therapy.[4] In an intravascular ultrasound study, it was found that underexpansion of drug-eluting stents caused stent thrombosis.[19] In another study, stent length along with heavy thrombus load and dissection was claimed to be the most important cause of intraprocedural stent thrombosis.[20] Late or disturbed endothelialization or widespread remodeling were shown to contribute to late stent thrombosis in animal studies.[21] Late endothelialization, impaired platelet aggregation and clumping, late stent malapposition, aneurysm formation, localized hypersensitivity due to stent polymers increase stent thrombosis risk in drug-eluting stents.[7,22]

The risk for stent thrombosis can be decreased with appropriate dose and duration of dual antiplatelet therapy. The lowest clopidogrel loading dose should be 600 mg, followed-by a maintenance dose of 75 mg/day for at least 6 to 12 months. Acetylsalicylic acid 100 mg/day should be used lifelong. Guidelines of the European Society of Cardiology recommend dual antiplatelet therapy for 6 to 12 months as class I indication for drug-eluting stents.[23]

In conclusion, late stent thrombosis seems to be closely related with the duration of antiplatelet therapy, but optimal duration of antiplatelet therapy has yet to be determined.

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