

## Very late drug-eluting stent thrombosis in a patient with an INR of 4.4

INR'si 4.4 olan bir hastada çok geç dönem ilaç salınımlı stent trombozu

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Duration of dual antiplatelet therapy after drug-eluting stent implantation is still an important issue awaiting a definite answer. A 50-year-old male patient was admitted with acute-onset chest pain and was diagnosed to have acute anterior myocardial infarction due to very late stent thrombosis. He had a 38-month history of two sirolimus-eluting stent implantation in the proximal left anterior descending (LAD) coronary artery. He had been on warfarin along with clopidogrel 75 mg/day until he decided to cease clopidogrel before a minor dental procedure 10 days before. Findings of physical examination and laboratory tests were normal except for an INR value of 4.4. After a loading dose of 300 mg clopidogrel, he was immediately taken to the catheterization laboratory. Angiography of the left system showed total occlusion of the proximal LAD with a thrombus at the level of the proximal stent. He was successfully revascularized without any complication and was discharged free of symptoms.

**Key words:** Coronary restenosis; coronary thrombosis/etiology; stents/adverse effects; thienopyridines; warfarin.

Bright days for drug-eluting stents (DES), which proved to be very effective in decreasing restenosis rates compared to bare metal stents, have been dramatically clouded by increasing number of cases with late stent thrombosis. The majority of cases are associated with abrupt cessation of thienopyridines, namely clopidogrel. In this report, we presented a patient who experienced very late thrombosis more than three years after DES implantation. He had been using warfarin with an INR of 4.4 and ceased clopidogrel in the past 10 days.

### CASE REPORT

A 50-year-old male patient was admitted to our clinic with acute-onset chest pain of two hours and was diagnosed as having acute anterior myocardial infarction

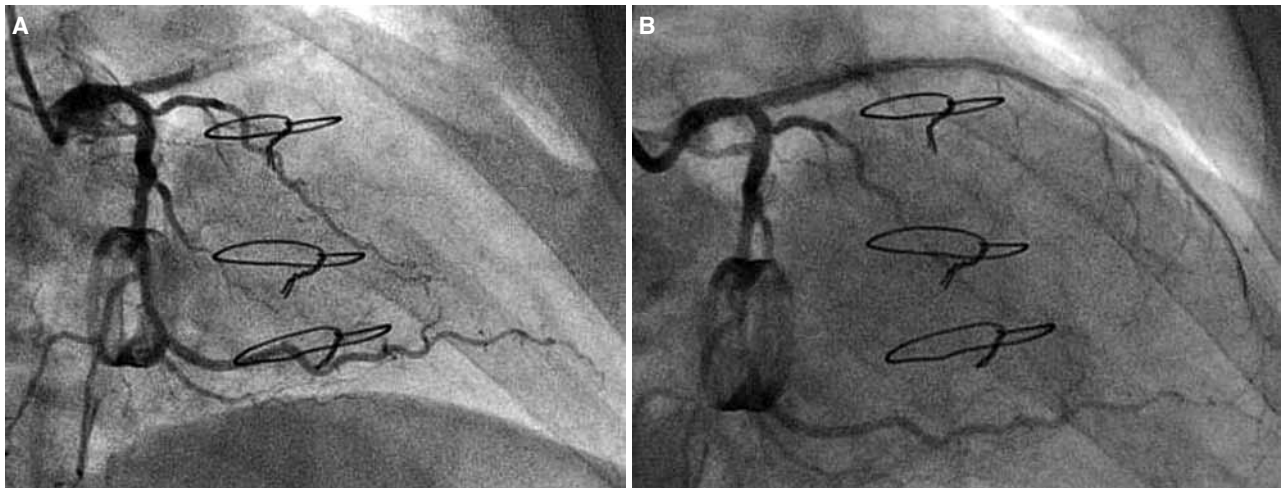
ilaç salınımlı stent yerleştirme sonrası ikili antitrombosit tedavinin ne kadar sürdürüleceği hala kesin yanıt bekleyen önemli bir konudur. Elli yaşında erkek hasta ani başlangıçlı göğüs ağrısıyla yatırıldı ve çok geç dönem stent trombozuna bağlı akut anterior miyokart enfarktüsü tanısı kondu. Hastaya 38 ay önce sol ön inen koroner arter proksimaline iki adet sirolimus salınımlı stent yerleştirilmişti. Düzenli olarak warfarin ile birlikte 75 mgr/gün klopidogrel tedavisi gören hasta, 10 gün önce basit bir diş tedavisi nedeniyle klopidogrel kullanmayı bırakmıştı. Fizik muayene bulguları ve laboratuvar testleri, INR değerinin 4.4 olması dışında normaldi. Hastaya 300 mgr klopidogrel yükleme dozu verildi ve acil olarak kateter laboratuvarına alındı. Sol sistem anjiyografisinde, proksimal stent bölgesinde sol ön inen arter proksimalinde tam tıkanıklık görüldü. Başarılı revaskülarizasyon işlemi sonrasında hasta semptomsuz olarak taburcu edildi.

**Anahtar sözcükler:** Koroner tekrarlayan darlık; koroner tromboz/etyoloji; stent/yan etki; tienopiridin; warfarin.

due to very late stent thrombosis. He had a 38-month history of two overlapping sirolimus-eluting stent (CYPHER Select, Cordis, Johnson & Johnson, FL, USA) (2.75 x 13 mm and 2.75 x 18 mm) implantation in the proximal left anterior descending (LAD) coronary artery for unstable angina in another medical facility. He was an ex-smoker and had had hypertension for the past five years. In addition, when he was asymptomatic with dual antiplatelet therapy, he underwent mitral valve replacement after a complicated percutaneous mitral valvuloplasty procedure in another clinic. The reason why he had not undergone coronary artery bypass grafting combined with mitral valve replacement could not be understood due to incomplete medical history and lack of documentation. After the operation, he took warfarin along with clopidogrel 75

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**Figure 1. (A)** Total occlusion of the proximal left anterior descending artery by a thrombus at the level of the proximal Cypher stent. **(B)** Complete revascularization of the thrombotic occlusion by percutaneous balloon angioplasty with no residual stenosis.

mg/day regularly and ceased aspirin. He was doing well since then, until he decided to cease clopidogrel before a minor dental procedure 10 days before. Findings of physical examination and laboratory tests were unexceptional except for an INR value of 4.4. After a loading dose of 300 mg clopidogrel, he was immediately taken to the catheterization laboratory. Angiography of the left system revealed that the proximal LAD was totally occluded with a thrombus at the level of the proximal stent (Fig. 1a). The length of the overlapping stent segment was 2-3 mm. The thrombotic lesion was crossed with a 0.014 inch IQ floppy guide wire (Boston Scientific, MA, USA) and dilated using a Viva 2.5 x 20 mm PTCA catheter (Boston Scientific) at 14 atmospheres. As acute angiographic result appeared satisfying without a significant residual stenosis (Fig. 1b), the procedure was ended without further stenting and tirofiban was started. He was discharged from the intensive care unit five days later with combination of clopidogrel 75 mg/day and warfarin. He was completely free of symptoms and of ischemia on testing at one-month visit.

## DISCUSSION

Drug-eluting stents have been developed and demonstrated to be very effective in decreasing restenosis and revascularization rates compared to bare metal stents.<sup>[1]</sup> However, there has been accumulating data also suggesting an uncomfortably increasing trend in late stent thrombosis rates, which is regarded as the "Achilles' heel" for these devices. Stent thrombosis, especially in the acute phase, has been a well-known and feared complication since introduction of coronary stents. Introduction of DESs to clinical practice

has changed the natural course of this dreadful complication, with more appearing lately over 1-4 years after implantation.<sup>[2,3]</sup> Lack of antiplatelet activity due to delayed re-endothelialization worsened by early cessation of clopidogrel is most commonly reported in thrombosis cases associated with DES, but there are many other predisposing factors such as long lesions, overlapping and small-diameter stents (as in our case), malapposition, multivessel interventions, geographical miss, uncovered dissections, end-stage renal disease, and diabetes.<sup>[4,5]</sup> Concerns about the contribution of late thrombosis to late mortality<sup>[6]</sup> have recently become less owing to long-term findings of recent randomized clinical trials.<sup>[5]</sup>

Many medications in the past were tried to stop, or at least substantially decrease this dreadful event, but none succeeded in bringing its rate down to an acceptable level. Thrombosis rates were about 16-20% with aspirin, dipyridamole, and dextran at the beginning of the stenting era,<sup>[7,8]</sup> then decreased to 3% with warfarin,<sup>[9]</sup> which is still considered too high for a general recommendation. Thienopyridines, especially clopidogrel, combined with aspirin have been demonstrated to be very effective in preventing this mortal complication and much debate still continues on when to stop clopidogrel in DES-bearing patients.

Despite significantly increased risk for bleeding, dual antiplatelet treatment combined with warfarin seems to be the best option for patients who are in need of continuous anticoagulation.<sup>[10]</sup> In our case, extremely high level of anticoagulation due to warfarin overuse was not sufficient to prevent the development of DES thrombosis after stopping clopidogrel, which underlines the importance of continued antiplatelet

activity in the presence of abnormal endothelium. Cessation of anticoagulants along with continuation of antiplatelet medications could be the ideal clinical decision, especially prior to dental procedures which are very commonly encountered in daily real-life practice.

In conclusion, antiplatelet medications (clopidogrel if possible) with/without warfarin should not be ceased at least one year after the implantation of a DES in patients undergoing minor surgery, elective or otherwise, unless it is absolutely contraindicated. Likewise, the use of a DES is not recommended in patients who require long-term anticoagulation.

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