Very late stent thrombosis after discontinuation of clopidogrel therapy

Rohit Barthwal and Brian A Herman

Stent thrombosis is an infrequent but severe complication after coronary stent implantation. Dual antiplatelet therapy has markedly reduced the occurrence of this potentially catastrophic event. The optimal duration of clopidogrel therapy in patients with drug-eluting stents is unknown. We describe a case of stent thrombosis 9 days after discontinuation of clopidogrel therapy, more than 3 years after placement of drug-eluting stents. (MJA 2008; 189: 229-230)

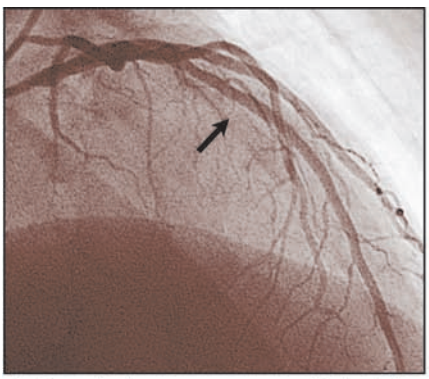
Clinical record

A 60-year-old man presented to his local community hospital with chest pain. He had had a percutaneous coronary intervention more than 3 years previously, when drug-eluting TAXUS stents (Boston Scientific Corporation, Natick, Mass, USA) were implanted in his left anterior descending coronary artery (LAD) and right coronary artery (RCA). Overlapping stents were placed in the LAD, measuring 2.5 × 16 mm and 2.5 × 8 mm, inflated to 1620.8 kPa. He had been taking aspirin and clopidogrel as dual antiplatelet therapy since that time. His past medical history included well controlled hypertension. At the time of presentation, he was haemodynamically stable, with normal resting electrocardiograms and normal troponin levels. As intermittent chest pain persisted despite medical management, he was transferred to an interventional centre for further investigations.

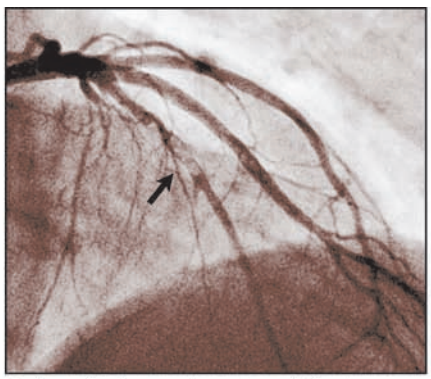
Coronary angiography showed mild irregularities of his LAD with widely patent stents in both the LAD (Figure, A) and RCA, with normal left ventricular function. There was no evidence of in-stent restenosis or disease adjacent to the stents. The next day, the patient developed abdominal pain associated with liver function test abnormalities indicative of cholestasis. Ultrasound of his abdomen showed multiple gall stones. It was thought likely that his chest pain was the result of his subdiaphragmatic disease. His clopidogrel therapy was stopped in anticipation of surgery, and he underwent a successful laparoscopic cholecystectomy. Five days later, he was discharged and clopidogrel therapy was not reinitiated.

The patient re-presented to his local hospital 4 days after discharge, with central chest pain. His electrocardiogram showed ST-segment elevation in the anterior leads, and reciprocal ST-segment depression in the inferior leads. In view of his recent surgery, he was not deemed a candidate for thrombolytic therapy, and was urgently transferred to our hospital.

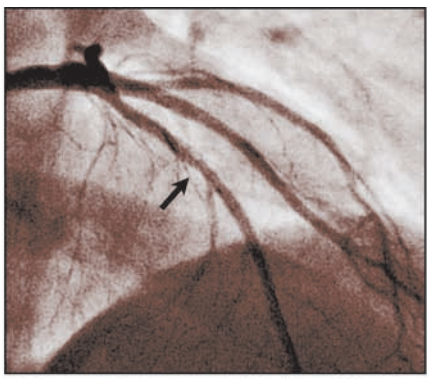
An angiogram showed thrombus within the stent in his LAD (1190 days after it was implanted), with slow antegrade filling of the distal vessel (thrombolysis in myocardial infarction [TIMI] grade 1 flow; Figure, B). His right coronary and circumflex arteries were normal, and a left ventriculogram showed severe hypokinesis of his apical wall. The clot was partially removed using a 6-French Export Aspiration Catheter (Medtronic Inc, Minneapolis, Minn, USA), and the artery was further dilated within the stent. No further stents were implanted. A small residual filling defect was noted after balloon angioplasty (Figure, C). Intravenous therapy with the glycoprotein IIb/IIIa inhibitor abciximab was initiated, and a loading dose of clopidogrel given. The period after percutaneous transluminal coronary angioplasty was uneventful, and the patient was subsequently discharged in a stable condition.



A: *Arrow indicates patent stents in the left anterior descending coronary artery.*



B: *Arrow indicates thrombus within the stent in the left anterior descending coronary artery.*



C: *Arrow points to a small residual filling defect after balloon angioplasty.* ◆

Discussion

Drug-eluting stents (DES) have been shown to be more effective than bare-metal stents (BMS) in reducing angiographic restenosis, by limiting intimal hyperplasia. This reduces the need for subsequent revascularisation procedures.[1-3] However, there is growing concern that delayed endothelisation and incomplete neointimal healing might lead to adverse cardiac outcomes and death as a result of late or very late stent thrombosis.[4,5] Mortality rates have ranged from 16% in a recent published registry from Spain documenting definite angiographic thrombus[6] to as high as 45% in another series including both definite and probable thrombosis.[7]

Stent thrombosis is an uncommon but life-threatening complication of stent implantation.[7,8] Stent thrombosis may be classified according to the time since implantation:[9] acute stent thrombosis occurs within 24 hours of the procedure; subacute stent thrombosis between 1 and 30 days after implantation; late stent thrombosis between 1 month and 1 year after implantation; and very late stent thrombosis more than 1 year after the procedure. The cumulative incidence of stent thrombosis with DES at 9–12 months has ranged from 0.5% to 1.5%, which is comparable to stent thrombosis with BMS,[10,11] with an incidence as high as 0.6% per year thereafter.[12] Recent clinical trials and registries have raised concern over increased rates of very late stent thrombosis with DES.[10,13,14] The cessation of dual antiplatelet therapy has been implicated as a pathophysiological factor in late and very late stent thrombosis.[7,11,15] Incomplete endothelisation of the metal struts because of the antiproliferative properties of the drug has also been implicated.[7,12,15] Mechanical factors involved in stent thrombosis have included malapposition of the stent to the vessel wall when originally implanted, and late malapposition because of retraction of the vessel wall during vessel remodelling.[11,12] Whether this is related to the drug, polymer, or stent platform itself is unknown.[12] The optimal duration of dual antiplatelet therapy after DES placement is still unknown. Current guidelines recommend clopidogrel therapy for at least a month and ideally up to a year with BMS, and for at least a year for patients treated with DES after hospitalisation for an acute coronary syndrome.[16] However, reports of very late cardiac events among patients with DES, particularly in relation to stent thrombosis and cessation of clopidogrel therapy, have cast doubt on these recommendations.[10,17,18] A recent observational study comparing DES with BMS suggested that clinical events related to late stent thrombosis in patients with DES after the discontinuation of clopidogrel therapy might limit the benefit of DES.[10]

Though there have been similar case reports,[17,18] ours is a unique example of an angiographically proven very late stent thrombosis, 3 years after placement of DES. During angiography 9 days prior to the event, no abnormality was noted within the previously implanted DES, nor at the stent edges before the cessation of clopidogrel therapy. Nine days after stopping therapy with this drug, filling defects were seen (Figure, B).

This case highlights the concerns about the duration of clopidogrel therapy following implantation of DES. It also raises the question of whether life-long clopidogrel therapy may be warranted in some patients.

Competing interests

None identified.

Author details

Rohit Barthwal, MB BS, FRACP, Advanced Cardiology Trainee
Brian A Herman, MD, PhD, FACC, Director of Interventional Cardiology
Launceston General Hospital, Launceston, TAS.
Correspondence: rohitbarthwal@rediffmail.com

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