CASE REPORT

An atypical presentation of an extremely late stent thrombosis after more than 7 years (2634 days) of DES implantation in a patient without obvious risk factors on regular dual antiplatelet therapy

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SUMMARY

Very late stent thrombosis is a rare complication of percutaneous coronary intervention in the era of dual antiplatelet therapy. The risk factors for stent thrombosis are drug default, age, diabetes, renal dysfunction, left ventricular dysfunction, smoking or procedure-related factors and complications. We are describing the case of a 55-year-old non-smoker patient without the conventional risk factors for stent thrombosis maintaining good compliance with dual antiplatelet (aspirin and clopidogrel) drugs in standard doses. The patient had a history of having received a Cypher stent more than 7 years (2634 days) ago in the left circumflex artery for the management of in-stent restenosis of a bare metal stent implanted previously. He was referred with acute stent thrombosis with an atypical presentation of non-ST elevation myocardial infarction having unexplainable spontaneous resolution of electrocardiographic changes. The patient was successfully managed with newer generation drug-eluting stents reimplantation. The presence of acute onset of symptoms and thrombus containing soft lesion as documented during intervention supported the diagnosis of acute stent thrombosis. To the best of our knowledge this case is one of the longest duration of presentation with acute stent thrombosis after stent implantation ever reported in literature and is also unique in its unusual mode of presentation.

renal dysfunction, left ventricular dysfunction or procedure-related complications and inappropriate stent selection and deployment including residual thrombus and dissection, long and complex lesions or antiplatelet drug resistance.¹

This case has a few unique aspects which deserve to be highlighted and brought to the notice of physicians and cardiologists dealing with such cases, the most important of which the fact that the event was extremely late after the intervention and occurred after more than 7 years after the intervention which is one of the longest interval ever reported. The other unusual facts are the occurrence of STh in a patient on regular dual antiplatelet therapy in the form of standard doses of aspirin and clopidogrel with no obvious conventional risk factors which have been described to be associated with STh. The presentation of STh with non-ST elevation myocardial infarction with no chest pain and a completely normalised ECG pattern in the absence of any recanalisation or collateralisation of the infarct-related vessel, makes this case unique. The importance of this case lies in the fact that STh presenting extremely late and with an atypical presentation as in our case can be easily missed by the primary care physicians which may lead to delay in administration of appropriate treatment which could be vital in salvaging the threatened myocardium.

BACKGROUND

Stent thrombosis (STh) is a well-known complication of percutaneous coronary intervention and most of the events occur early in the course of follow-up of such cases. In the era of highly effective antiplatelet, pleotropic and negative remodelling drugs, this complication is seldom reported and has a shown a dramatic decrease in its incidence. STh is predominantly seen early in the course of follow-up after the intervention with the majority of the cases occurring in the first day or the first month or so. Most cases of STh are seen in patients with a history of default of antiplatelet therapy or premature dose reduction by their treating physicians or cardiologists for various reasons including non-cardiac surgeries or in presence of bleeding-related complications of antiplatelet therapy. Rare cases of STh have been described after 1–2 years of stent implantation. The various other risk factors which have been incriminated to cause STh are age, diabetes,

CASE DESCRIPTION

A 55-year-old individual presented with symptoms of unexplained lethargy and anxiety since the past 2 h with no chest pain, dyspnoea, perspiration or left upper limb paraesthesia. An ECG was performed by the referring physician as a part of evaluation as the patient had a significant history of coronary artery disease and had undergone percutaneous intervention and stent implantation previously. The patient had been compliant with the dual antiplatelet therapy (150 mg of aspirin and 75 mg of clopidogrel) which had been prescribed to him in 2007 when he was treated with a Cypher stent for restenosis of a bare metal stent in left circumflex artery (LCX).

INVESTIGATIONS

The ECG showed ST segment depression in inferolateral leads (figure 1). The symptoms were retrospectively suspected to be anginal equivalents on

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Figure 1 The ECG at presentation showing transient stent thrombosis segment changes in inferolateral leads.

account of the transient ECG changes which were present at that time.

The patient was shifted to our centre as the centre where the patient had been first evaluated had no facility for an angiogram. The patient was absolutely asymptomatic at the time of presentation at our centre and the ECG changes had completely normalised within a span of less than an hour from the previous ECG (figure 2). The vitals were stable.

The echocardiogram revealed new onset of regional wall motion abnormality in the inferoposterior region. These changes were presumed to be of new onset as there was no prior history of any infarction in this territory and both the previous interventions were performed for management of exertional symptoms. This hypothesis is also supported by the fact that there were no pre-existing ECG changes in the inferior leads (figures 1 and 2). The cardiac enzymes including creatine Kinase MB (88 ng/mL) and the troponin (2.36 ng/mL) performed after 8 h of the onset of the symptoms were positive in high titres.

The angiogram which was performed immediately revealed acute STh of the Cypher stent (2.5×20 mm) which had been implanted in the LCX for the treatment of in-stent restenosis in 2006 (2634 days ago) for a bare metal stent which was implanted in 1999 (2.25×15 mm). The occlusion of the vessel appeared acute and there were no collaterals and hence the reason of complete normalisation of the ECG changes and resolution of symptoms could not be explained (figure 3, videos 1–3). Genetic evaluation of the patient for clopidogrel responsiveness was not performed in this case as the patient was now planned for further treatment with prasugrel and so the test would have had no clinical significance in further patient management.

TREATMENT

The patient was treated with an emergency percutaneous coronary intervention using a 0.014" floppy wire and the lesion was extremely soft and wire could be crossed across the lesion easily. This aspect of the thrombus containing lesion along with the

Figure 2 The ECG at presentation at our hospital which had completely normalised with no ST segment changes as were present earlier and neither any signs of infarction.

Figure 3 A figure illustrating the occluded stent with no antegrade or collateral flow in the territory supplied by left circumflex artery.

acute onset of ischaemic symptoms supports that there was an acute ST. The lesion was predilated with a 2.5×15 mm balloon at 8 atmospheres. The vessel was stented with a 2.75×25 mm Everolimus eluting stent and discharged with prasugrel and aspirin. The idea of prescribing prasugrel in this patient was that the patient required a stronger antiplatelet drug than the one he was already on which could further decrease the chances of stent thrombosis (figure 4, videos 4 and 5).

OUTCOME AND FOLLOW-UP

The patient has been stable at 10 months of follow-up and has not shown any subsequent episodes suggestive of any ischaemic event.

DISCUSSION

STh is an important and life-threatening complication of percutaneous coronary intervention but the incidence has dramatically decreased in the era of dual antiplatelet agents. The most

Video 2 Angiogram in RAO cranial view showing an the occluded stent with no collateral from the left system.

common reason which is reported to predispose most cases of STh are related to drug default or premature termination of dual antiplatelet therapy due to planned or unplanned non-cardiac surgery or due to bleeding related side effects of antiplatelet therapy.²⁻⁴ The case reported by us was surprising in terms of the extremely rare presentation of the patient with acute STh (after 2634 days of implantation) while the patient being regularly on dual antiplatelet therapy (150 mg of aspirin and 75 mg of clopidogrel). Surprisingly this patient had almost no other obvious risk factors for STh. The only possible risk factor which might be considered important in this case was the fact that the patient had thrombosis in a stent which was deployed for the treatment of in-stent re-stenosis for a bare metal stent which had been implanted around 9 years ago. The angiograms which were performed during stent implantation were not available for comparison neither was any subsequent angiogram performed in the intervening period as the patient had been completely asymptomatic. Hence, whether any immediate or delayed stent mal-apposition was present as a risk factor or not cannot be commented on.

There have been several studies which have attempted to assess the causes and incidence of STh. DESERT (Drug Eluting

Video 1 Angiogram in RAO caudal view showing complete occlusion of the stent with no antegrade flow or any filling from collaterals.

Video 3 Right coronary angiogram showing absence of any collateralisation to the LCX territory.

Figure 4 A still from the angiogram showing good antegrade flow after the percutaneous coronary intervention to the left circumflex artery.

Stent Event Registry of Thrombosis) was the largest multicenter, observational, case-control registry which has addressed this issue. This study was designed to assess the incidence of STh in patients who had been previously treated with drug-eluting stents. A total of 922 patients were enrolled and a retrospective analysis was performed.⁵ In this registry it was reported that 75% of late STh were seen to occur within 1 year of stent deployment. The clinical presentation of late STh was predominantly in the form of myocardial infarction of which 66.9% of the patients presenting with elevation of the STh segment.

STh has been reported to occur at 17 months⁶ and more recently in another case report as late as 26 months after deployment of a sirolimus eluting stent.⁷

In another series of patients Ong *et al*⁶ had reported the incidence of late STh to be 0.35% in a cohort of 2006 patients who had received a DES. These patients were followed up for a median duration of 1.5 years. During this study a total of eight cases of late STh were reported and confirmed angiographically. Three of these cases were reported in cases in which antiplatelet

Video 4 Angiogram with stent in situ across the LCX during the PCI.

Video 5 Angiogram in a magnified view showing good antegrade flow in the LCX territory with no residual stenosis.

therapy was stopped totally while two cases occurred within a month after clopidogrel was stopped with the continuation of aspirin, and the rest of the cases occurred several months (ranging between 2 and 23 months) after being put on a single antiplatelet agent.

In the RAVEL study the incidence of late stent mal-apposition was found to be 21% of the compared to only 4% in the control arm hence proving late stent mal-apposition could be a potential predisposing factor for delayed STh.⁷

Another very surprising aspect of this patient's presentation was that he presented with no chest pain with only symptoms of anxiety and lethargy which were retrospectively considered to be angina equivalents and the ECG at presentation had completely normalised in comparison to the ST-T changes in the ECG which was recorded prior to presentation at our hospital (figures 1 and 2). The mechanism of spontaneous resolution of ECG changes to a completely normal state in presence of an acute infarct in the inferoposterior region in the absence of vessel recanalisation or collateral formation as documented by the angiogram is difficult to explain. This also is a caution to be vigilant for all the treating physicians who may have easily missed this

Learning points

- ▶ Very late thrombosis has been previously reported at various time intervals but the occurrence after more than 7 years is an extremely rare occurrence and possibly the longest ever described in a patient on regular dual antiplatelet therapy.
- ▶ The other surprising element of this case was the fact that the patient had almost none of the traditionally described risk factors for stent thrombosis which is also an aspect which is important to be kept in mind by the clinicians who deal with such cases.
- ▶ The presentation of acute stent thrombosis with complete resolution of symptoms and completely normalised ECG in the absence of any collateral formation or recanalisation of the infarct related vessel is extremely unlikely and calls for high index of suspicion in diagnosis of such cases.
- ▶ A 'missed diagnosis' or a 'misdiagnosis' in such cases could be life threatening and could also be sinister to the long-term prognosis of patients with acute stent thrombosis leave alone the medicolegal implication of these cases. This adds more to the importance of this case in terms of education of the clinicians and the cardiologists dealing with such cases.

potentially life-threatening condition and the patient could have been left untreated in the presence of an ongoing infarction.

This is thereby an important aspect of presentation of acute STh which needs to be kept in mind and calls for a high index of suspicion which forms the key to a correct diagnosis in such cases.

Competing interests None.

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