OMCR

OMCR 2015 1 (3 pages)
doi:10.1093/omcr/omu063

Case Report

Eculizumab treatment for paroxysmal nocturnal haemoglobinuria in a patient with recurrent simultaneous multivessel coronary stent thrombosis

Giovanni Luigi De Maria, Rizwan Sarwar and Adrian P. Banning*

Oxford Heart Centre, Oxford University Hospitals, Oxford, UK

*Correspondence address. The John Radcliffe Hospital, Headley Way, Headington, Oxford OX3 9DU, UK.
Tel: 08165 228934; Fax: 01865 220585; E-mail: adrian.banning@ouh.nhs.uk

Received 5 November 2014; revised 17 December 2014; accepted 20 December 2014

We describe a case of recurrent multivessel coronary stent thrombosis in the absence of the typical hallmarks of this phenomenon: (i) discontinuation or poor compliance with double antiplatelet therapy; (ii) stent malapposition and (iii) stent underexpansion. In this case, the recurrence of stent thrombosis was indeed manifestation of a more complex underlying disease, and eventually allowed the clinicians to come to the final diagnosis of paroxysmal nocturnal haemoglobinuria.

INTRODUCTION

Stent thrombosis is the most feared complication after coronary stent implantation, although its incidence has been reduced by potent antiplatelet therapy, improvements in stent design and procedural technique [1]. Occasionally, stent thrombosis can also be a 'symptom' of an underlying disease process as in the presented case.

CASE REPORT

A 70-year-old man presented as an emergency with chest pain and infero-posterior ST elevation. He had a previous history of chronic aplastic anaemia for which he had received high-dose steroid therapy with remission many years earlier.

He had undergone percutaneous coronary intervention (PCI) with stenting to the left anterior descending artery (LAD) 5 years ago. This procedure was complicated by a small post-procedural stroke. One month earlier, he had been referred to another hospital with a non-ST-elevation myocardial infarction (NSTEMI) and underwent further PCI to LAD and first obtuse marginal (OM1) with implantation of two everolimus drug-eluting stents [Promus Premier 3.5 × 12 mm (Boston Scientific, Natick, MA, USA) in both LAD and OM1]. He had been discharged on aspirin and prasugrel, but was readmitted a week later with stent thrombosis [2] affecting both LAD and OM1 stents. He was treated with thrombus aspiration, abciximab infusion and 48 h of intravenous heparin but 10 days after discharge, then admitted to our institution with a further infero-posterior STEMI.

Immediate coronary angiogram demonstrated simultaneous recurrent stent thrombosis of both LAD and OM1 stents (Fig. 1a). Thrombus aspiration, abciximab infusion and dilation with a semi-compliant balloon (1.5 × 15 mm and 3.0 × 20 mm) restored TIMI III flow within OM1, whereas thrombus aspiration and abciximab infusion re-established flow within the LAD. However, residual haziness was noted within both stents (Fig. 1b). After 4 days of intravenous heparin infusion, a repeat angiogram (Fig. 1c and d) with fractional flow reserve (FFR) and intravascular ultrasound (IVUS; Fig. 1e–g) was performed. Results were satisfactory in the LAD with an FFR of 0.84 (thus excluding significant residual ischaemic burden) and well-apposed stents were visualized in both LAD and OM1 using IVUS (Fig. 1 e, f, h and i). However, IVUS showed a critical residual stenosis in the OM1 due to high residual thrombus (minimal lumen area 2.5 mm^2; Fig. 1i). Further dilation to the stent in OM1 was then performed with a 3.5 × 15 mm non-compliant balloon with reasonable final results.

Although the procedure was uncomplicated, approximately 20 h later, the patient presented a new cerebral transient ischaemic accident with evidence of infarct in the right medial and left posterior cerebral artery territories on a cerebral CT scan.

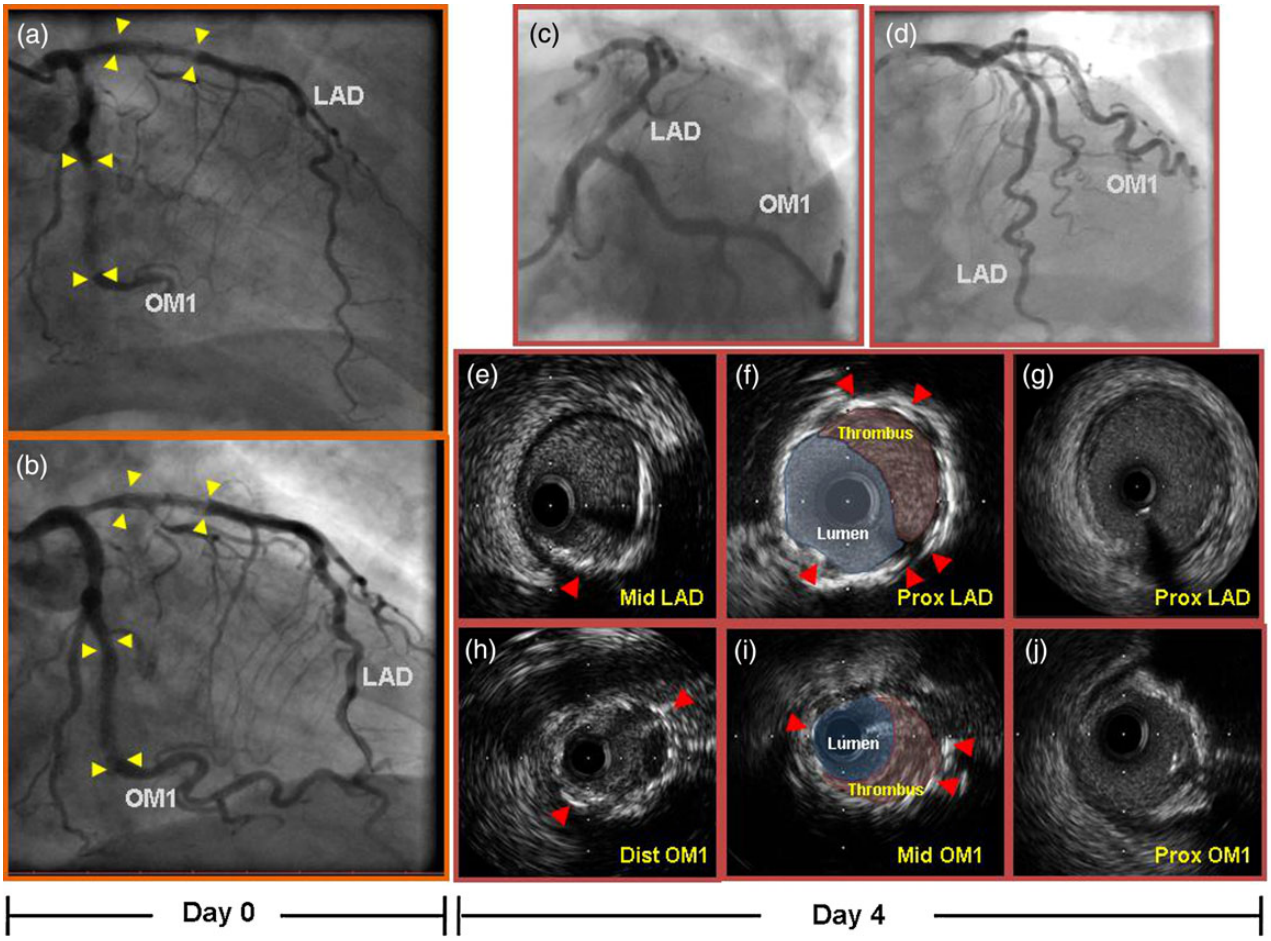

Figure 1: Coronary angiography shows simultaneous stent thrombosis on LAD and OM1 (**a**) and restoration of good flow after thrombus aspiration, GPIIbIIIa inhibitor infusion and dilation with a semi-compliant balloon (**b**; yellow arrowheads highlight stent edges). Coronary angiography after 4 days of heparin infusion showed reasonable good results on both LAD and OM1 (**c** and **d**). IVUS showed well-stent strut apposition (red arrowheads; **e**, **f**, **h** and **i**) in both vessels with residual thrombotic material (pink area; f and i), causing a significant reduced minimal lumen area on OM1 (i).

Full compliance with antiplatelet agents both prior in the community, and during hospital admission, was confirmed. Interestingly, a history of sporadic episodes of dark urine was reported by the patient's family.

Investigations showed that the lactic dehydrogenase was raised at 640 UI/l, associated with a low haemoglobin (11 g/dl), with a high reticulocyte count (3.1%). A large expanded clone of blood cells with deficient expression of CD59 and CD55 was detected, leading to a diagnosis of paroxysmal nocturnal haemoglobinuria (PNH). Treatment with eculizumab (anti-C5 monoclonal antibody) was initiated immediately, and the patient was discharged on aspirin and ticagrelor, with an uneventful recovery confirmed 6 months later.

DISCUSSION

PNH is a rare haematological disease (1–2 cases per million) [3] due to a somatic mutation of the PIG-A gene responsible for the synthesis of the glycophosphatidylinositol (GPI), which is a membrane anchor for a large group of surface proteins [4]. In PNH, blood cells present a deficit of GPI and thus of CD55 and CD59, which are regulators of complement cascade. CD55 is indeed involved in regulating the activity of C3 and C5 convertases, whereas CD59 controls the final steps of the complement cascade, by preventing the incorporation of C9 into the C5b–8 complex, thus inhibiting the assembling of the membrane attack complex [5]. As a consequence, blood cells, and mainly erythrocytes, present a dramatic susceptibility to the complement cascade. Haemolysis and recurrent thrombosis, mainly in the venous system, are the main clinical manifestations of this disease [4].

In this case, a series of components suggest the 'very unusual' nature of the stent thrombosis. First, the lack of dual antiplatelet discontinuation and the absence of stent underexpansion/malapposition exclude the two main risk factors that predispose to stent thrombosis [6]. Second, the long history and the dramatic recurrence of cardiac and cerebrovascular events suggest a possible thrombophilic condition. Third, the patient had a previous history of aplastic anaemia, which is often associated with PNH [7]. Urgent treatment with eculizumab resolved a catastrophic clinical scenario, characterized by

life-threatening thrombosis despite optimal contemporary anti-thrombotic agents.

ACKNOWLEDGEMENT

We owe a special thanks to Prof. Peter Hillmen, St. James's University Hospital, Leeds, UK.

CONFLICT OF INTEREST STATEMENT

None declared.

REFERENCES

1. Claessen BE, Henriques JP, Jaffer FA, Mehran R, Piek JJ, Dangas GD. Stent thrombosis: a clinical perspective. *JACC Cardiovasc Interv* 2014;**7**:1081–92.
2. Cutlip DE, Windecker S, Mehran R, Boam A, Cohen DJ, van ES GA, *et al.* Clinical end points in coronary stent trials: a case for standardized definitions. *Circulation* 2007;**115**:2344–51.
3. Parker C, Omine M, Richards S, Nishimura J, Bessler M, Ware R, *et al.* Diagnosis and management of paroxysmal nocturnal hemoglobinuria. *Blood* 2005;**106**:3699–3709.
4. Kelly R, Richards S, Hillmen P, Hill A. The pathophysiology of paroxysmal nocturnal hemoglobinuria and treatment with eculizumab. *Ther Clin Risk Manag* 2009;**5**:911–21.
5. Hill A, Richards SJ, Hillmen P. Recent developments in the understanding and management of paroxysmal nocturnal hemoglobinuria. *Br J Haematol* 2007;**137**:181–92.
6. Parodi G, La Manna A, Di Vito L, Valgimigli M, Fineshi M, Bellandi B, *et al.* Stent-related defects in patients presenting with stent thrombosis: differences at optical coherence tomography between subacute and late thrombosis in the Mechanism of Stent Thrombosis (MOST) study. *Eurointervention* 2013;**9**:936–44.
7. Maciejewski JP, Sloand EM, Sato T, Anderson S, Young NS. Impaired hematopoiesis in paroxysmal nocturnal hemoglobinuria/aplastic anemia is not associated with a selective proliferative defect in the glycosylphosphatidylinositol-anchored protein-deficient clone. *Blood* 1997;**89**:1173–81.