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Early restenose in a polymer-free Biolimus A9-coated stent (BioFreedom): A case report based on optical coherence tomography☆

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ABSTRACT

An 81-year-old male patient with a severe de novo coronary artery stenosis in the proximal left anterior descending artery was treated with a BioFreedom stent (3.5 × 11 mm), three months later, the patient was re-admitted with chest pain and slightly increased troponin. The angiogram showed a significant in-stent restenosis in the recently treated lesion. Optical coherence tomography revealed a fully expanded stent without areas of incomplete stent apposition. Severe immature neointimal hyperplasia without formation of thrombosis was visualized, causing a severe in-stent restenosis. An underlying plaque rupture within the mid-proximal part of the in-stent restenosis was evident.

1. Introduction

At present, percutaneous coronary intervention (PCI) with drug-eluting stent (DES) implantation is the standard strategy to treat coronary artery disease in institutions around the world. However, concerns regarding long-term safety of first generation DES have prompted to development of novel DES systems such as the polymer-free Biolimus A9 coated stent (BioFreedom) (Biosensors Inc., Newport Beach, CA). In the current case report we present a patient with an early in-stent restenosis after implantation of a BioFreedom stent, and supplementary intracoronary imaging with optical coherence tomography (OCT) is used to shed light on the underlying mechanism.

2. Case report

An 81-year-old man was admitted to the department of cardiology due to intermittent chest pain. The patient was previously known with ischemic heart disease and earlier coronary artery bypass grafting (CABG) with a left internal mammary artery (LIMA) to the ramus diagonalis and triple saphenous vein grafts to the right coronary artery, to the left circumflex artery and to the ramus intermedius had been performed back in 1993. The patient had a previous history of arterial hypertension, dyslipidemia and was an earlier smoker. He had no history of diabetes mellitus, neither no known family history of ischemic heart disease. Following CABG, the patient was asymptomatic for many years. One week prior to admission to our hospital the patient developed chest pain and the general practitioner referred him for a diagnostic elucidation at our department. The electrocardiogram (ECG) revealed anterior ST-segment depressions and biochemically troponin I was moderately elevated (143 ng/L), why the patient was diagnosed as having a non ST-segment elevation myocardial infarction (NSTEMI). Following a loading dose of 180 mg of ticagrelor and 300 mg of aspirin, dual antiplatelet therapy (DAPT) with ticagrelor 90 mg twice daily and aspirin 75 mg once daily was ordained. The patient was referred for a subacute coronary angiogram, which revealed a 90% single de novo stenosis in the proximal left anterior descending artery (LAD) (Fig. 1). The patient was treated a BioFreedom stent and a 3.5 × 11 mm stent (Fig. 1B). The LIMA to the ramus diagonalis and all 3 vein grafts were angiographically well-functioning.

Three months post-PCI of the proximal LAD, the patient started to experience shortness of breath during physical activity, and complaints of chest pain began to evolve. The patient was re-hospitalized. Troponin I was discreetly increased and ECG revealed unchanged anterior ST-segment depressions. There had been no interruption in DAPT. A repeat subacute coronary angiogram showed a significant in-stent restenosis at the newly LAD-stented segment (Fig. 2). A supplementary OCT (C7 Dragonfly, LightLab Imaging Inc., Westford, MA, USA) was performed in order to investigate the underlying mechanism of the early in-stent restenosis (Fig. 3a). OCT images revealed a fully expanded stent without areas of incomplete stent apposition in its entire length. Severe immature neointimal hyperplasia without formation of thrombosis was visualized, causing a severe in-stent restenosis with a minimal lumen area (MLA) of 2.1 cm^2. An underlying plaque rupture within the mid-proximal part of the in-stent restenosis

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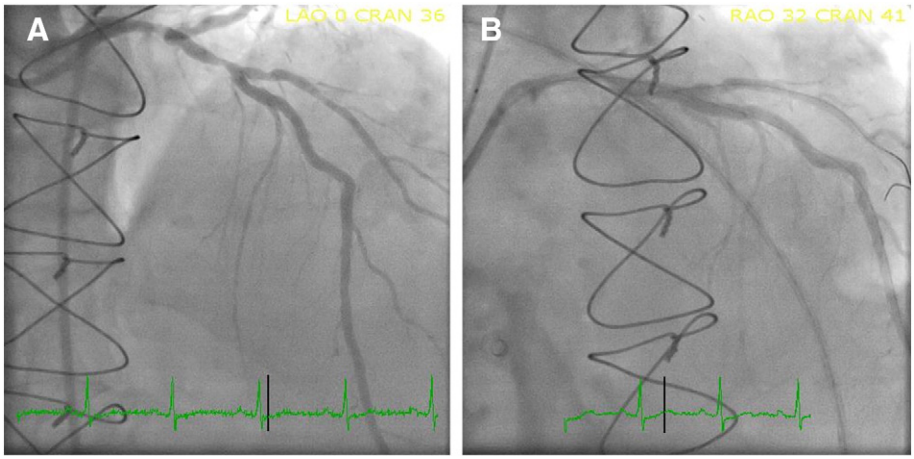

Fig. 1. A Baseline coronary angiography showing a 90% stenosis in the left anterior descending (LAD) artery. **B** Successful implantation of a 3.5 × 11 mm BioFreedom stent without angiographically signs of residual stenosis.

was evident. Repeat revascularisation with PCI and implantation of a 3.5 × 12 mm Promus Stent (Everolimus-eluting stent, Boston Scientific, Malborough, MA) overlapping the previous BioFreedom stent was performed in order to cover and repeal the early in-stent restenosis. Repeat OCT post-procedure showed optimal stent expansion and apposition without residual protruding material or edge dissections (Fig. 3b). Fig. 4 shows supplementary OCT images of clinically asymptomatic left main (LM) stenosis.

3. Discussion

Although first generation sirolimus- (SES, Cypher) and paclitaxel- (PES, Taxus) eluting stents have radically reduced the incidence of in-stent restenosis and the need for target lesion revascularization (TLR) in comparison with bare-metal stents (BMS) in randomized clinical trials, in-stent restenosis still occurs in approximately 5%–10% of DES-treated PCI-cases [1]. The safety of the first generation DES was also limited by delayed arterial healing and incomplete strut endothelialization, leading to an increased risk of late and very late thrombosis [2]. Both SES and PES used durable thick polymer to carry and control the release of their antiproliferative agents. The permanent presence of these polymers has been associated with chronic inflammation, hypersensitivity responses, and local toxicity within the arterial vessel walls [3–6]. As a consequence, the focus of clinical research has been on the development of novel drug carrier systems including biodegradable polymers and non-polymeric stent surfaces [7]. In the development of polymer-free DES-systems, it has been important to modify the surface of the stent platform that is carrying and controlling the release of the antiproliferative drug. The BioFreedom Drug-Eluting Coronary Stent Delivery Systems (Biosensors Inc., Newport Beach, CA) is composed of 3 key components, including a 316 L stainless steel platform that has been modified with a proprietary surface treatment using a micro abrasion process, resulting in a selectively microstructured, abluminal surface. The microstructured surface allows the antiproliferative drug, Biolimus A9, to adhere to the abluminal surface of the stent without the use of a polymer or binder. Biolimus A9 is a highly lipophilic, semisynthetic sirolimus analogue [7]. A previous preclinical, randomized study compared BioFreedom ("high-dose" and "low-dose") stents with SES and BMS histomorphometrically and histologically at 28 and 180 days in the coronaries of mini-swine models. At 28 days, there was a significant reduction in neointimal proliferation with BioFreedom ("high-dose" and "low-dose") stents and SES compared with BMS. At 180 days, BioFreedom (both "high-dose" and "low-dose") stents were associated with reduced neointimal proliferation, whereas both SES and BMS exhibited increased neointima. BioFreedom stents showed decreased fibrin deposits and inflammation, including granuloma and giant cells, compared with SES, and delayed healing

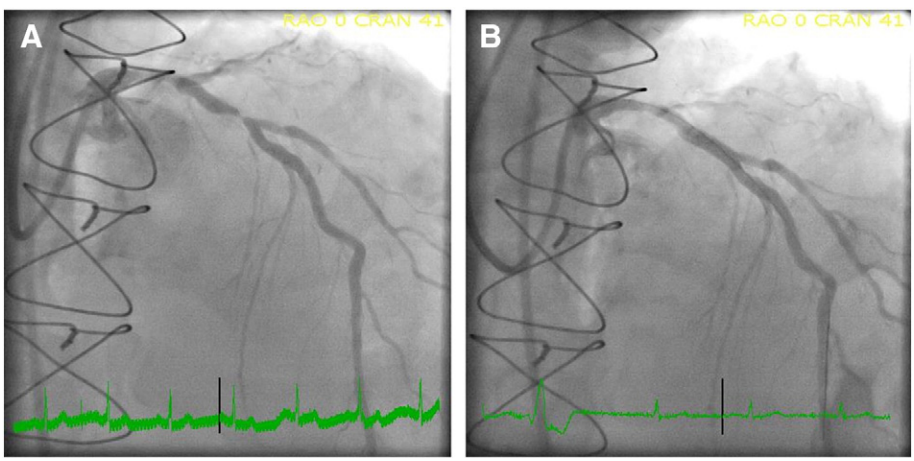

Fig. 2. A Repeat coronary angiography 3 months after LAD-stenting showing a significant instent restenosis. **B** Repeat revascularisation was performed with implantation of a 3.5 × 12 mm Promus Stent.

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