Case Report

Avastin-Eluting Stent: Long-Term Angiographic and Clinical Follow Up

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The detection of atheromatous lesions in patients with coronary artery disease is related to neovascularisation, since it is associated with the presence of a dense network of *vasa vasorum* in the vascular wall. The increased density of *vasa vasorum* causes destabilisation of the atheromatous plaque. The safety and efficacy of a stent coated with bevacizumab, a monoclonal antibody for vascular endothelial growth factor have been established at both the experimental and the clinical level. We present the case of a patient with acute myocardial infarction and significant stenosis in the mid-section of the left anterior descending coronary artery, treated by implantation of a bevacizumab-coated stent. A coronary angiographic examination 2 years later showed patent coronary arteries with a well-preserved angioplasty result in the anterior descending artery. This is the first report of findings beyond six-month follow up of this type of stent and represents the first clinical and angiographic proof of its long-term efficacy.

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Atheromatosis is associated with neovascularisation, as a dense net of *vasa vasorum* develops in atheromatic arterial wall.[1] The increased density of *vasa vasorum* in unstable atherosclerotic plaques promotes the vulnerability of the plaques.[2] The safety and efficacy of a dedicated stent against neovascularisation has been established both in experimental studies and in the preliminary results of a clinical study. The 6-month angiographic follow-up results were recently reported.[3] We report the first patient with 2 years of clinical and angiographic follow up after avastin-eluting stent implantation in the middle segment of the left anterior descending coronary artery (LAD).

Case presentation

A 61-year-old male with a medical history of arterial hypertension and dyslipidaemia was admitted to our hospital because of exercise-induced chest pain radiating to his back and his left arm. The patient had experienced the symptoms for one month before his admission and in all cases the pain diminished at rest. The electrocardiogram at the time of admission showed sinus rhythm with ST-T segment depression, and T-wave inversion in leads I, aVL, V_3-V_6. Cardiac ultrasound showed normal myocardial wall motion, without findings of valvular heart disease. Cardiac enzymes, measured twice (troponin I, CK, CK-MB, ALT, AST) were within normal limits. During hospitalisation the patient started treatment with nitrates, aspirin, metoprolol, atorvastatin, ramipril and clopidogrel. On the second day, he underwent coronary angiography. A significant lesion was identified in the middle segment of the LAD, producing a stenosis of 80%. In the right coronary artery an eccentric severe lesion with thrombus and an associated stenosis of 95% was found in the proximal segment. The lesion in the right

Pre DES

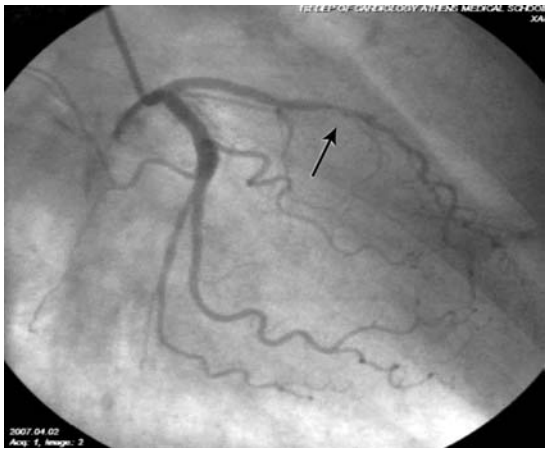

Figure 1. Coronary angiography showing the lesion in the left anterior descending artery.

Post DES

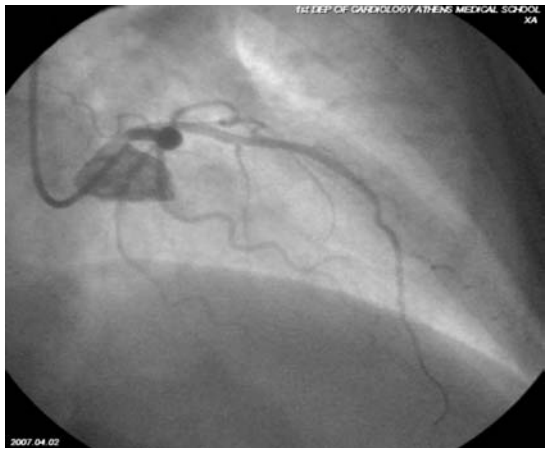

Figure 2. Coronary angiography of the left anterior descending artery after stent implantation.

coronary artery was considered to be the culprit lesion and was treated successfully by the implantation of a conventional stent. The non-culprit lesion in the LAD (Figure 1) was scheduled to be treated with an avastin-eluting stent.

Loading bevacizumab stents

The procedure of loading avastin on the stent has been described previously in detail. Briefly, a BiodivYsio stent delivery system (Biocompatibles Ltd., London, UK) was used. The stent is a laser cut, stainless steel stent coated with phosphorylcholine. The biocompatible phosphorylcholine coating forms a double layer of synthetic material that absorbs a drug via a "sponge-like" mechanism.[4]

The stent was immersed into a solution of 4 ml avastin (25 mg/ml, Roche) for 5 min. Then the stent was removed from the solution and after it was allowed to dry for 1 min, 10 μl of the same solution was pipetted onto the stent. The stent was again allowed to air-dry for 1 min. This process was repeated with an additional 5 min of air-drying.

After the preparation the avastin-eluting stent was successfully implanted in the target lesion without residual stenosis (Figure 2). The patient was discharged 2 days later with double antiplatelet therapy, together with metoprolol, atorvastatin and ramipril. Clopidogrel was discontinued by protocol at 12 months. During the 2 years of clinical follow up the patient remained asymptomatic. Repeat coronary angiography was performed at 2 years. The stented segment was free of any intimal hyperplasia as estimated by angiography and showed minimal late loss (0.28 mm, Figure 3).

Discussion

Vascular endothelial growth factor (VEGF), is a potent regulator of physiological and pathological angiogenesis. It is therefore a potential therapeutic target for the inhibition of plaque neovascularisation, in which it plays a major role.[5] Bevacizumab, a recombinant humanised monoclonal antibody against VEGF, has been applied in oncology as a potent anti-angiogenic agent, and has been recently used successfully in the from of a bevacizumab-eluting stent for the treatment of non-culprit *de novo* lesions in patients suffering acute coronary syndromes.[6,7]

Follow-up

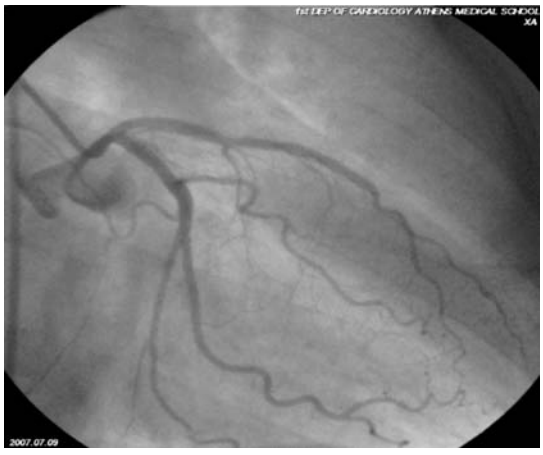

Figure 3. Coronary angiography at follow up.

We used the BiodivYsio stent for local delivery of bevacizumab at the target lesion, as this stent has been used successfully in previous studies for delivering possible anti-hyperplastic agents. After experimental evaluation of the method,[8,9] we recently proceeded to the clinical application of this stent in 20 patients, with a follow-up period of 6 months. According to our results, the bevacizumab-eluting stent is safe for the treatment of non-culprit *de novo* lesions in patients suffering from acute coronary syndromes.[3] The minimal neointimal hyperplasia, observed by intravascular ultrasound, confirmed the experimental results, in which the mean neointimal thickness and area were less in the bevacizumab group than in the control group.[8] Although the mean neointimal hyperplasia area was greater compared with other drug eluting stents, such as sirolimus[4] and paclitaxel-eluting stents,[10] it was less than that of bare metal stents.[3]

In other studies with phosphorylcholine-coated stents the patients did not receive prolonged antiplatelet therapy;[11-14] however, our patients were treated with double antiplatelet medication for a period of 12 months in order to avoid any thrombotic events. The clinical follow up of these patients showed that even after the discontinuation of clopidogrel at 6 months late thrombosis was not observed up to 9 months.[3]

This is the first case to be presented with long-term clinical and angiographic data from a patient treated with a bevacizumab-eluting stent. Despite the discontinuation of clopidogrel at 12 months, there was no late stent thrombosis or stenosis after 24 months' follow up, indicating the long-term safety of this stent. However, further clinical follow up of patients already treated with bevacizumab-eluting stents is required for a fuller evaluation of the safety of the devices.

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