Long-term results of drug-eluting and bare metal intracoronary stent implantation in the same heart transplant recipient: a case report

Długoterminowe wyniki porównania stentów uwalniających leki i metalowych implantowanych u tego samego pacjenta po transplantacji serca – opis przypadku

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Abstract

Transplanted heart coronary artery disease (TxCAD) occurs in over 40% of orthotopic heart transplant (OHT) recipients and remains the leading cause of late post transplant mortality. The diffuse and distal character of TxCAD stenoses results in difficulties in selection of appropriate treatment methods.
Restenosis is the main factor limiting the long-term effectiveness of PCI in TxCAD. We present a case of a TxCAD patient with the left main coronary artery (LM) stenosis covering also proximal parts of the left anterior descending artery (LAD) and circumflex branch of the left coronary artery (Cx) treated simultaneously by drug-eluting stent (DES) and bare-metal stent (BMS) implantation. Significant restenosis was observed 6 months after BMS implantation in proximal Cx, while there was no restenosis in DES placed in LM and LAD revealed during 4-year follow-up.
Key words: transplanted heart coronary artery disease, percutaneous coronary intervention (PCI), drug-eluting stent (DES), bare-metal stent (BMS), restenosis.

Streszczenie

Choroba tętnic wieńcowych przeszczepionego serca (ang. *transplanted heart coronary artery disease* – TxCAD) występuje u ponad 40% pacjentów po transplantacji serca i stanowi wiodącą przyczynę późnej śmiertelności po zabiegu. Rozsiany charakter zmian w tętnicach przeszczepionego serca, najczęściej zlokalizowanych dystalnie, utrudnia wybór optymalnej metody leczenia. Restenoza stanowi zasadniczy czynnik ograniczający długoterminową skuteczność angioplastyki w tej grupie pacjentów. W pracy przedstawiono przypadek pacjenta z TxCAD obejmującą pień lewej tętnicy wieńcowej, proksymalną część gałęzi międzykomorowej przedniej (ang. *left anterior descending artery* – LAD) i gałęzi okalającej (ang. *circumflex branch* – Cx) lewej tętnicy wieńcowej. Pacjentowi wszczepiono równocześnie stent metalowy (ang. *bare metal stent* – BMS) i uwalniający leki (ang. *drug-eluting stents* – DES). Istotną restenozę zaobserwowano już 6 miesięcy po implantacji BMS w Cx. Nie zaobserwowano restenozy po implantacji DES w LM ani LAD podczas 4-letniej obserwacji pacjenta.
Słowa kluczowe: choroba tętnic wieńcowych przeszczepionego serca, przezskórna interwencja wieńcowa, stent uwalniający lek, stent metalowy, restenoza.

Introduction

In patients who underwent orthotopic heart transplantation (OHT), allograft coronary artery disease (TxCAD) remains the main cause of long-term graft failure [1-3]. Results of numerous TxCAD-addressed studies agree that it eventually develops in over 40% of cases [4-7]. Pathologic examinations reveal diffuse, intimal proliferation foci, leading to concentric occlusions, primarily in distal vessels [2]. Multiple factors are believed to contribute to its occurrence, such as immunosuppressive regimen, viral infections, donor age and presence of acute rejection episodes [8].

TxCAD symptoms, due to denervation of the graft, are usually atypical or completely absent [9]. It may present

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as a congestive heart failure, arrhythmia or sudden death. Cases presenting typically, with angina or acute myocardial infarction, are very rare [9-11].

Studies suggest that proper pharmacological management: statins and anti-hypertensive treatment may prevent or delay the occurrence of TxCAD. Likewise, the use of modern immunosuppressive agents (mycophenolate mofetil, sirolimus) contributes to TxCAD prevention. Still, the treatment of already established TxCAD is a major challenge in post-OHT patient management [12, 13].

The assessment of bare-metal (BMS) vs. drug-eluting stents (DES) was a subject of many studies. Still, a possibility of BMS and DES comparison in identical conditions (same patient, coronary artery, and implementation date) is an uncommon opportunity.

We present a case of OHT recipient transplanted and followed in the Silesian Center for Heart Disease showing significant LM stenosis in coronary angiography treated by means of percutaneous coronary intervention (PCI) with simultaneous DES and BMS implantation in LM and proximal parts of LAD (DES) and Cx (BMS).

Case report

A 42-year-old male patient underwent OHT in December 1992 due to post-ischemic heart failure, with no complications. His immunosuppression protocol consisted of cyclosporine A, azathioprine and steroids. Since 1998 he has been administered 20 mg of simvastatin daily. In 1998, he was diagnosed with type II diabetes. His antiplatelet treatment was started after the diagnosis of TxCAD and consisted of aspirin 75 mg daily (since PCI performed in 1999) and ticlopidine 250 mg twice a day (2004-2007) eventually replaced by clopidogrel 75 mg daily.

He was free from TxCAD, proven by systematic coronary angiography assessment, until 1999 when he was treated by means of PCI of circumflex branch (Cx) of the left coronary artery (due to early restenosis, BMS was implanted within 24 hours after the primary procedure). Subsequent coronary angiographies have shown no signs of stenosis for the following 3 years, when significant 70% in distal left main coronary artery (LMCA) and critical left anterior descending artery (LAD) stenosis was observed. Due to the patient's general well-being and expected high periprocedural risk of surgical or percutaneous revascularization, no invasive treatment was undertaken at this time. The patient was discharged with a limited physical activity recommendation until further angiographic control.

There was no progression of patient's TxCAD until March 2003, when he was admitted for a scheduled follow-up. On admission the patient was in a very good condition,

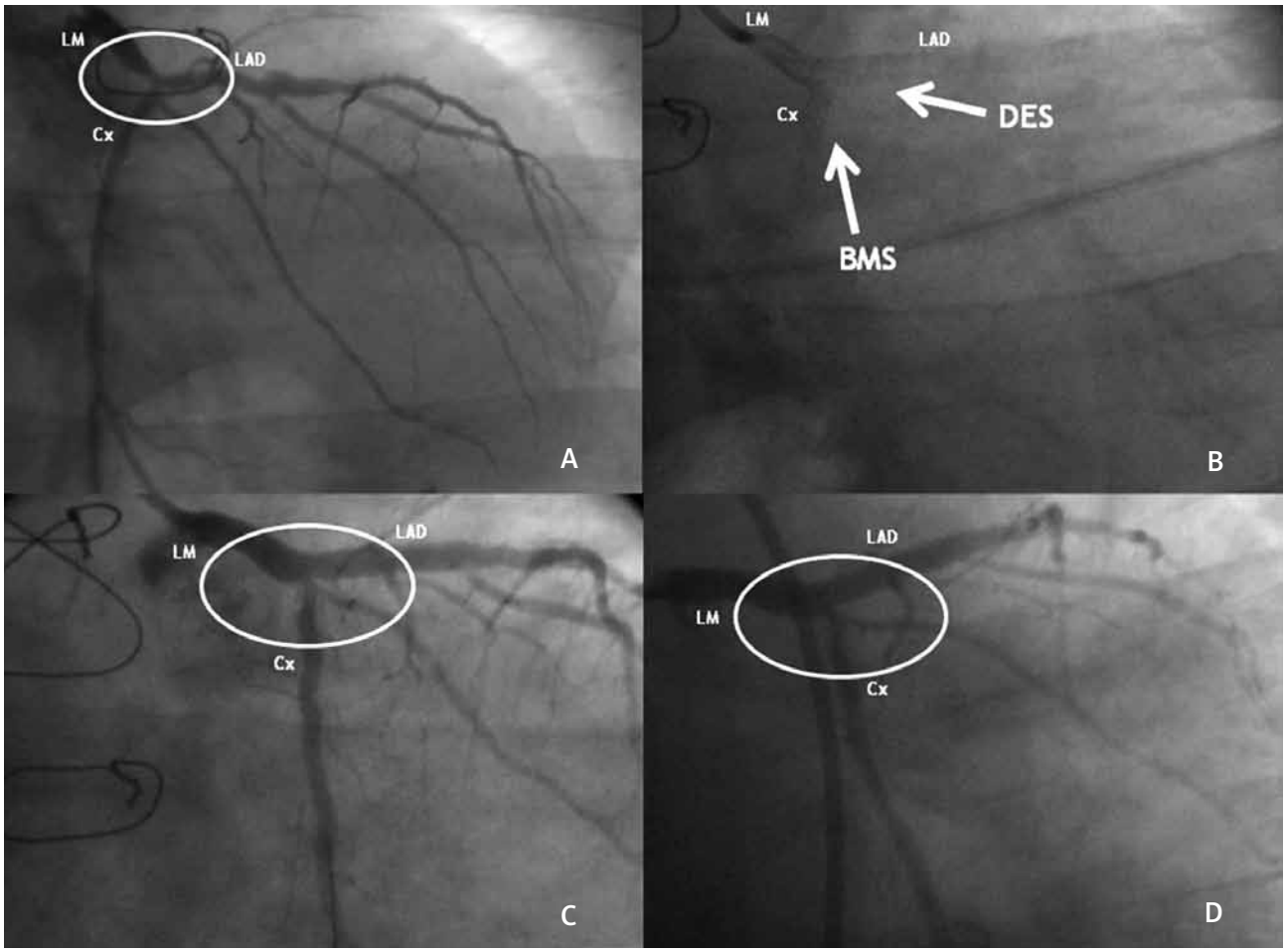

Fig. 1A.–D. Coronary angiographies (description in the text)

hemodynamically stable, with no signs of decreased graft function and free from any stenocardial symptoms. Echocardiography revealed proper function and size of the left ventricle. Nonetheless, the following coronary angiography revealed further progression of LAD stenosis. Under such circumstances, percutaneous transluminal coronary angioplasty (PTCA) was performed with BMS implantation into LAD. At balloon inflation the patient experienced typical stenocardial chest pain, proving the cardiac allograft's reinnervation. The discomfort was relieved after balloon deflation. Troponin and CK-MB levels were not elevated. Further in-hospital stay of the patient was uncomplicated.

In March 2005, the patient was admitted for standard follow-up and underwent another coronarography. The patient complained of irregular heartbeat. The assessment of previous 24 h ECG recordings confirmed an increased number of ventricular extrasystoles. The coronarography showed LM over Cx and LM over LAD critical (95%) stenoses as well as Cx and LAD in-stent restenosis (Fig. 1A). A team of interventional cardiologists and cardiac surgeons has opted for percutaneous treatment. The restenoses were treated by PTCA. Mi-Jazz 3.0 × 20 mm BMS was implanted in the LM over Cx and a CYPHER 3.5 × 33 mm DES was implanted in the LM over LAD stenosis (Fig. 1B). Both stents were inflated with the kissing-balloon method, resulting in complete vessel dilatation. No symptoms of ischemia were observed. Further in-hospital stay was uncomplicated.

During five years of follow-up the patient was under a standard post-OHT coronarographic regimen. Mild restenosis (30%) was observed in the LM over Cx (BMS) location in December 2005, June 2008 and January 2009. Critical restenosis in Cx developed in December 2007 (Fig. 1C). No signs of restenosis were observed in the LM over LAD location, where DES was implanted till the last angiography performed in June 2010 (Fig. 1D).

Discussion

TxCAD, along with graft rejection, is the leading cause of cardiac allograft function loss. It usually presents as diffuse, distal vessel stenoses. Its complex pathogenesis, along with comprehensible difficulties of PCI treatment stress the importance of the proper pharmacological approach in order to prevent or delay the manifestation of TxCAD [12].

Cardiac retransplantation remains the only definite solution for TxCAD, with satisfactory results in patients with chronic graft failure [14]. However, it is a highly limited option due to insufficient number of donors and poorer graft survival in comparison to primary transplantation [15]. High peri-operative risk, unsatisfactory long-term survival and frequent necessity of intravascular interventions limit the use of coronary artery bypass grafting (CABG) in cardiac allograft vasculopathy [16, 17].

This leads to PCI becoming a dominant therapeutic method in TxCAD patients, especially with focal narrowings of proximal vessels [15]. Although not common, involvement of major coronary arteries, such as LMCA, may also be observed, with possible prognosis similar to this of typical atherosclerotic disease. CABG, despite being the standard option for primary LMCA involvement, is regarded as a high-risk procedure in TxCAD. Under such circumstances, PCI, while burdened with some disadvantages – high risk of restenosis in post-OHT patients stealing the spotlight – may be seen as an attractive therapeutic option [18, 19].

Restenosis is the main factor limiting the long-term effectiveness of PCI. Although the use of DES does not seem to reduce patient mortality [20, 21], there is a number of recent studies showing that the use of DES significantly decreases the risk of restenosis [9, 20, 22, 23].

The possibility of long-term comparison of BMS and DES in one patient, simultaneously implanted to a large vessel (LMCA) is uncommon. The case of our patient shows a definite advantage of DES vs. BMS. Fully aware of the fact that large trials do not confirm mortality reduction [20, 21], we would like to underline that every possibility of restenosis risk reduction can be vital, especially in main coronary arteries. This position is supported by the International Society for Heart and Lung Transplantation in its current guidelines [24].

Higher long-term mortality rates in heart transplant recipients with TxCAD, regardless of proper, systematic angiographic surveillance, can be associated with the graft's denervation. Atypical course of coronary artery disease, often completely asymptomatic, may lead to a graft failure or sudden cardiac death. There are only a few published reports of symptomatic angina and/or AMI in post-OHT patients, most of which were successfully managed by means of PCI. Although our patient was one of the rare examples of graft reinnervation, the possibility of asymptomatic severe ischemia occurrence is a strong indication that the reduction in restenosis risk, especially in LMCA, should be a major concern during post-OHT PCI procedures.

Conclusion

Our observation with over 5 years of follow-up suggests that even complex PCI associated with the application of drug-eluting stents to reduce the risk of restenosis in large vessel stenosis is the optimal solution both in terms of safety and effectiveness in patients with advanced TxCAD.

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