Takayasu Arteritis and Left Main Disease Treated with Zotarolimus Drug-Eluting Stents, after Paclitaxel-based Angioplasty and The Use of Sirolimus

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ABSTRACT
A case of Takayasu arteritis with left main disease is described. Intrastent restenosis occurred one year after the first percutaneous coronary angioplasty (PCI) with a drug-eluting stent (everolimus). After suppression of the active disease with immunosuppressive therapy, and sirolimus added, a second PCI were performed with zotarolimus-based DES, after pre-dilatation with paclitaxel-based balloon angioplasty. Control coronary angiography with optic coherence tomography performed two months later confirmed no restenosis. This is the first case of effective local use of two different antiproliferative agents during angioplasty and effective systemic use of sirolimus in Takayasu’s disease with coronary involvement.

Keywords
Takayasu arteritis, Chest pain, Angioplasty, Prednisone, Vessels.

Introduction
We report a case of Takayasu arteritis with left main disease successfully treated with zotarolimus-based drug-eluting stent, after pre-dilatation with paclitaxel-based angioplasty and the use of sirolimus.

Case Presentation
A 26-year-old woman known with Takayasu arteritis was admitted to the emergency department with atypical chest pain. She had no known cardiovascular risk factors. Her medication included methotrexate 25mg/week, prednisone 5mg/day and tocilizumab every week. After an abnormal stress test, an angiogram was performed in January 2016 and showed a 65% stenosis of the left main. Percutaneous coronary angioplasty (PCI) with a drug-eluting stent (everolimus) was realized, with IVUS control showing good stent deployment. At discharge, ASA 80mg/day, ticagrelor 90mg twice daily, bisoprolol 5mg/day and atorvastatin 80mg/day were added to her usual medications.

She consulted again in February 2017 with recurring angina during the weaning of her prednisone. Following a doubtful stress echocardiography, a cardiac CT angiogram showed intra-stent restenosis of the left main extending to the left anterior descending artery and the circumflex (Figure 1A-B).

Figure 1A: Cardiac CT angiogram showed intra-stent restenosis of the left main extending to the left anterior descending artery.

Figure 1B: Cardiac CT angiogram showed intra-stent restenosis of the left main extending to the proximal circumflex.

Positron emission tomography (PET-Scan) was performed and suggested active vasculitis of the thoracic aorta as well as active inflammation of the left main. Control angiogram confirmed significant restenosis at the former site of the stent in the left main, encompassing the proximal circumflex.
After multi-disciplinary discussion, an increase in immuno-suppression is then attempted to douse the disease’s activity before any reintervention. The patient received 500mg IV of solumedrol for 3 days followed by prednisone 50mg/day and sirolimus orally. A PET-Scan performed 10 days later demonstrated resolution of the inflammation of the left main. Optical coherence tomography (OCT) pre-PCI showed intimal fibrotic thickening without atheromatous plaque, concordant with the underlying inflammatory disease (Figure 2A). A percutaneous intervention with zotarolimus-based drug-eluting stents was performed at the left main and the circumflex after pre-dilatation with paclitaxel-based balloon angioplasty. OCT post-PCI showed good stents expansion, no malposition, nor thrombus or dissection (Figure 2B). Control coronary angiography with OCT performed two months later confirmed the absence of restenosis. The patient remained asymptomatic six months after.

**Figure 2A:** OCT pre-PCI showed intimal fibrotic thickening without atheromatous plaque.

**Figure 2B:** OCT post-PCI showed good stent expansion.

CT = computerized tomography, OCT = optical coherence tomography, PCI = percutaneous coronary intervention

### Discussion

Takayasu arteritis is a chronic inflammatory vasculitis affecting mainly large vessels, with coronary involvement in 10% of patients, with left main implication in 50% of cases. Cardiac manifestations include angina in 90% of cases [1]. Active inflammation at the time of percutaneous or surgical intervention increase the risk of complications by seven times [2].

Principles of treatment include the use of corticosteroids and conventional immunosuppressive agents such as methotrexate, azathioprine, cyclophosphamide and mycophenolate mofetil to suppress systemic and vascular inflammation [3]. For refractory cases, use of biological agents is often necessary [4].

The optimal treatment of coronary artery disease in Takayasu arteritis is not yet well established. Yang and colleagues evaluated percutaneous versus surgical revascularization and demonstrated a higher incidence of long-term restenosis in patients with percutaneous coronary intervention [5].

We decided to proceed with percutaneous intervention in this patient with pre-dilation with drug-eluting balloon (paclitaxel) and dilation with drug-eluting stents (zotarolimus) comprising each different antiproliferative agents from the one used during the first angioplasty. This strategy of using two different antiproliferative agents had not been described in literature, but is based on rationale belief that combining different antiproliferative agents could further inhibit the fibrotic proliferation from the underlying inflammation in the arteries.

The mechanism of restenosis in patients with Takayasu disease is mainly intimal neoproliferation, and anti-proliferative therapy based on sirolimus has been attempted. In cardiac transplant recipients, sirolimus is used to decrease the incidence and progression of cardiac allograft vasculopathy, but its use in vasculitis has not been reported in the literature. To our knowledge, this is the first reported case of effective use of local and systemic anti-proliferative agents in Takayasu's disease with coronary artery disease.

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