Use of drug-coated balloon instead of drug-eluting stent for pediatric cardiac allograft vasculopathy

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ABSTRACT

Cardiac allograft vasculopathy (CAV) sometimes leads to restenosis, even after percutaneous transcatheter intervention. Recently, drug-coated balloons (DCBs) have been successfully used to treat coronary artery disease, especially CAVs, in adults. However, no studies have used DCBs in pediatric CAVs. We encountered a patient with CAV who underwent cardiac transplantation for restrictive cardiomyopathy at the age of 2 years. Nine years after the transplantation, severe stenosis of the proximal left anterior descending branch was observed. Considering the patient's young age and the possibility of restenosis, we performed an intervention with DCB. Follow-up conducted 7 months after the intervention showed no restenosis. Cardiac coronary artery lesions following transplantation are more likely to result in restenosis earlier than arteriosclerotic lesions. In pediatric patients, restenosis might require multiple stents and prolonged antiplatelet therapy. Our findings provide evidence supporting the possibility of an effective treatment of CAV in children.

Keywords: Cardiac allograft vasculopathy, drug-coated balloon, drug-eluting stent, pediatric heart transplantation, percutaneous coronary intervention

INTRODUCTION

Cardiac allograft vasculopathy (CAV) is a common cause of late mortality in pediatric transplantation patients. Severe coronary artery stenosis may warrant percutaneous coronary intervention (PCI); however, the diffuse progression of CAVs may eventually require re-transplantation.[1]

Drug-eluting stents (DES) are useful for CAV, but restenosis remains a major problem,[2] and repeated PCI may be required in some cases. Bypass surgery for CAVs is associated with a high perioperative mortality rate. Recently, drug-coated balloons (DCBs) have been successfully used for CAVs in adults.[3-5] Although some studies have reported on DCBs in children with pulmonary vein stenosis,[6] there are no reports on the use of DCBs in CAVs. We present the case of a pediatric patient with CAV who was treated by PCI using a DCB for severe stenosis following heart transplantation (HTx).

CLINICAL SUMMARY

An 11-year-old male patient underwent HTx abroad for restrictive cardiomyopathy at the age of 2 years, and immunosuppression was managed with tacrolimus (FK) and everolimus (EVL). He developed drug-induced renal dysfunction 3 years after HTx and received mycophenolate mofetil (MMF) to decrease the dose of FK, which was a major contributor to renal dysfunction. However, he developed interstitial pneumonia due to EVL and was eventually managed with FK and MMF. Subsequently, the renal failure worsened, leading to kidney transplantation

Access this article online

Quick Response Code:

Website: www.annalspc.com

DOI: 10.4103/apc.apc_47_22

How to cite this article: Hirose M, Narita J, Hashimoto K, Ishii R, Ishida H, Ozono K. Use of drug-coated balloon instead of drug-eluting stent for pediatric cardiac allograft vasculopathy. Ann Pediatr Card 2023;16:45-7.

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Submitted: 25-Mar-2022 **Revised:** 08-May-2022 **Accepted:** 08-May-2022 **Published:** 04-Apr-2023

9 years after HTx. The cardiac function was stable, and there were no signs of rejection during the annual cardiac catheterization. No ischemic symptoms or noticeable electrocardiogram changes were present. Periodic echocardiography 9 years after HTx also demonstrated good left ventricular function; however, we noted accelerated blood flow in the left anterior descending artery. Severe stenosis (90% blockage) was identified in the proximal left anterior descending branch on coronary angiography [Figure 1a], and the fractional flow reserve was as low as 0.64. Before the intervention, dual antiplatelet therapy was initiated (aspirin 100 mg/day and clopidogrel 75 mg/day). DES was an option, but considering his age and risk of future restenosis, we selected DCB (paclitaxel coated) to minimize the vessel wall damage and intimal proliferation. A 6-Fr sheath was introduced through the right femoral artery and vein, and 2000 U of unfractionated heparin was administered. After progressing to the left coronary artery with a 6-Fr Left Judkins Guiding Catheter and 6-Fr guide extension catheter and performing stepwise predilatation with Cutting Balloon (Flextome™ 2.0–10 mm and 2.25–10 mm, each in turn), DCB expansion (SeQuent® Expansion with 2.5–15 mm) was performed [Figure 1b]. Optical coherence tomography was used to confirm the expansion [Figure 2a and b]. Postoperative follow-up at 7 months revealed no restenosis and sufficient coronary artery patency [Figures 1c and 2c]. No hyperlipidemia or hypertension was noted, and the risk for emboli was low. Therefore, antiplatelet drugs were terminated.[2,3]

DISCUSSION

CAV is considered a chronic rejection reaction due to T-cell infiltration of the vessel walls. However, nonimmunological factors, such as hypertension and hyperlipidemia, have been reported as exacerbating factors of CAV. Although the prevalence of CAV is lower in pediatric patients than in adults, a 9-year multicenter study in pediatric recipients found a 50% graft survival rate at 2 years after severe CAV diagnosis, with a 24% mortality rate within 2 years for any patient who developed CAV.[7] Therefore, the prevention and treatment of pediatric CAV are important issues.

Anginal symptoms are often not observed in denervated transplanted hearts. Coronary angiography and intravascular ultrasound (IVUS) are important because of the risk of sudden death or ischemic events if there are no obvious ischemic changes on electrocardiography, as noted in this patient. Some institutes consider IVUS to be feasible for patients who weigh ≥10 kg; however, for patient safety, at our institute, IVUS is only performed for patients who weigh ≥20 kg. We believe that the 5-Fr guiding catheter, the minimum size required for IVUS, is excessively thick for pediatric coronary arteries. Unfortunately, at 11 years of age, the patient weighed

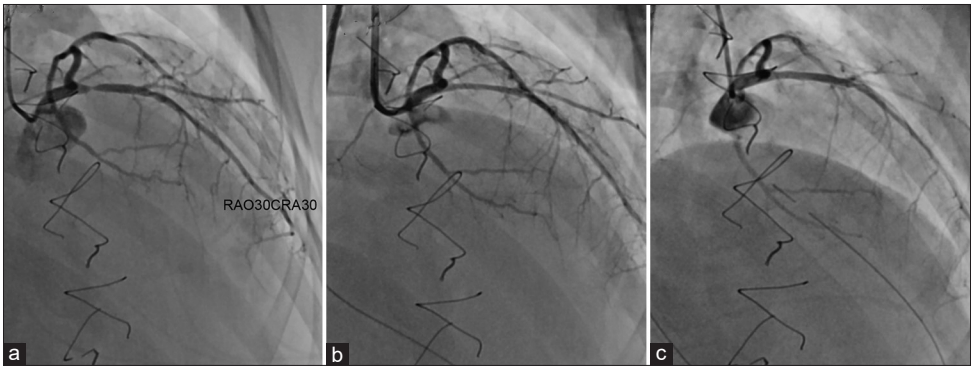

Figure 1: Coronary artery angiography shows coronary allograft vasculopathy. (a) Image taken before the intervention. (b) Image taken immediately after the intervention with a drug-coated balloon. (c) Image taken 7 months after the intervention

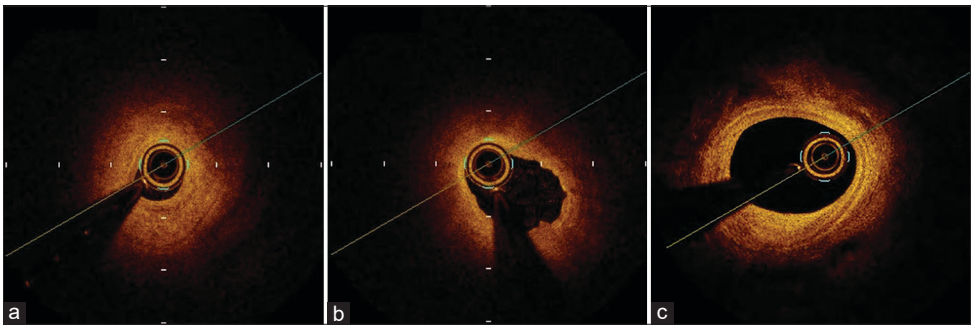

Figure 2: Optical coherence tomography images taken at the same time as coronary artery angiography. (a) Image taken before the intervention. (b) Image taken immediately after the intervention with a drug-coated balloon. (c) Image taken 7 months after the intervention

20 kg, which made him barely eligible for IVUS, and made it difficult to predict CAV progression.

PCI is an effective treatment option for proximal and localized CAV. In one of the few reports on PCI in pediatric CAV, severe stenosis recurred in 6/7 cases, thus warranting stent implantation. Three patients required re-transplantation, and three died in the early or mid-term;[8] therefore, the indications for stent implantation require thorough consideration.

Transplanted cardiac coronary artery lesions are more likely to develop restenosis earlier than arteriosclerotic lesions because lesion progression can be faster in the stented and nondwelling portions. For coronary artery disease patients with a history of transplantation, especially in childhood, multiple stents and prolonged antiplatelet therapy may be required. According to recent reports, revascularization can be safely performed without a stent in small vessels with a diameter <3 mm with atherosclerotic lesions, and dual antiplatelet therapy duration can be shortened.[9,10] EVL-eluting stents are an option in older patients, but close follow-up is warranted because of the risk of restenosis. Furthermore, the coronary artery size should increase with growth. Consequently, revascularization was performed with a paclitaxel-coated balloon, and good patency was confirmed in the medium term. One limitation is that we could not restart EVL or sirolimus due to the risk of interstitial pneumonia. Currently, coronary angiography and IVUS are scheduled at least annually.

In summary, to the best of our knowledge, there are no reports on revascularization with a DCB for CAVs in children. This is the first report of successful PCI with DCB for CAV following pediatric HTx. Our findings suggest the possibility of an effective treatment for CAV in children.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. The patient and his guardians have provided their formal consent for his images and other clinical information to be reported herein. They understand that his name and initials will not be published, and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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