

Percutaneous coronary intervention for coronary allograft vasculopathy with drug-eluting stent in Indian subcontinent: Issues in diagnosis and management

Mohammed Shakawat Alam, Arvind Sahadev Singh, Sreeja Pavithran, Vijayakumar Subban, Ajit Mulasari, Kothandam Sivakumar

Department of Cardiology, Madras Medical Mission, Chennai, Tamil Nadu, India

ABSTRACT

Coronary allograft vasculopathy fails to give a warning anginal pain due to denervation and often presents with acute coronary syndrome, ventricular dysfunction, or sudden cardiac death. Early diagnosis in a pediatric patient is difficult as it involves invasive coronary angiography or advanced imaging such as intravascular ultrasound or optical coherence tomography. A 12-year-old boy developed acute coronary syndrome, elevated troponins, and right bundle branch block, 5 years after cardiac transplantation and was treated with culprit-vessel angioplasty with a drug-eluting stent. Advanced imaging showed the involvement of nonculprit vessels too. In a detailed literature search, we failed to identify a similar clinical presentation and management in the subcontinent, hence our interest in publishing this report for educational value. Issues in diagnosis, management, prognosis, and prevention are discussed.

Keywords: Acute coronary syndrome, coronary allograft vasculopathy, drug-eluting stent, heart transplantation, pediatric cardiology, stent angioplasty

INTRODUCTION

Coronary allograft vasculopathy (CAV) is the leading cause of mortality after 1st year of heart transplantation.^[1] It is caused by “endothelial injury triggered by immunological mechanisms operating in a milieu of nonimmunologic risk factors.”^[2] Due to denervation of the heart, typical anginal symptoms do not occur, and coronary angiogram is needed for diagnosis. Angiography detects a 2%, 9%, and 17% incidence of pediatric CAV at 1, 3, and 5 years of transplantation, but intravascular ultrasound (IVUS) detects 75% by 5 years.^[3,4] A 12-year-old boy who underwent emergency heart transplantation for a large left ventricular fibroma at 7 years of age presented

with acute coronary syndrome, elevated troponins, and right bundle branch block, 5 years after the transplant. After coronary angiogram showed CAV involving three vessels, he was treated with culprit-vessel stent angioplasty. Issues in diagnosis, management, prognosis, and prevention are discussed in this first report of a successful percutaneous intervention for pediatric CAV in the Indian subcontinent.

CASE REPORT

A 12-year-old boy could not come off cardiopulmonary bypass after resection of a large left ventricular

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: Alam MS, Singh AS, Pavithran S, Subban V, Mulasari A, Sivakumar K. Percutaneous coronary intervention for coronary allograft vasculopathy with drug-eluting stent in Indian subcontinent: Issues in diagnosis and management. *Ann Pediatr Card* 2020;13:234-7.

Videos Available on: www.annalspc.com

Access this article online

Quick Response Code:



Website:

www.annalspc.com

DOI:

10.4103/apc.APC_69_19

Address for correspondence: Dr. Kothandam Sivakumar, Senior Consultant Cardiologist, Madras Medical Mission, Chennai - 600 037, Tamil Nadu, India.

E-mail: drkumarsiva@hotmail.com

Submitted: 14-May-2019

Revised: 24-Oct-2019

Accepted: 17-Mar-2020

Published: 02-Jun-2020

lateral wall fibroma. He underwent an emergency orthotopic heart transplant within 12 h of extracorporeal circulatory support. His posttransplant management included immediate basiliximab, followed by titrated tacrolimus, mycophenolate mofetil, prednisolone, aspirin, statins, prophylactic valganciclovir, and antifungal and antipneumocystis carinii drugs. The donor was a young teen who suffered neurotrauma without any cardiac ischemic insults. No donor-specific antibodies or panel-reactive antibodies were assessed in this emergency setting. The postoperative period was uneventful, and medications were titrated based on drug levels. His annual endomyocardial biopsy and coronary angiography were serially normal in the first 4 years [Figure 1 and Videos 1a and b, 2a and b, 3a and b]. His blood pressure, lipids, and glucose levels were normal, and there was no exposure to passive smoking.

He was hospitalized with an episode of syncope and showed new-onset right bundle branch block with inverted T waves and elevated troponins in triage and managed with dual antiplatelets and heparin. His coronary angiogram next day showed diffuse proximal, mid, and distal left anterior descending (LAD) coronary artery stenosis with proximal ramus disease. Even though the right coronary artery appeared normal on angiography, optical coherence tomography (OCT) showed diffuse intimal thickening more than 0.5 mm with intact internal elastic lamina of its entire length, thereby confirming

Grade III three vessel CAV [Figure 2]. There were no lipid plaques, foamy macrophages, or thrombus in the lesion. Guide catheter malalignment precluded the use of OCT in the left coronary artery [Figure 2]. There was no evidence of rejection on biopsy. Echocardiography confirmed normal left ventricular systolic and diastolic functions. As there was no preceding febrile illness or prodromes, cytomegaloviral screening was not done. He underwent stent angioplasty of proximal and mid LAD with Resolute Onyx (Medtronic, Santa Rosa, CA, USA) [Figure 3 and Video 3c]. Coronary angiography after 6 months showed patent stent and mild progression in the left circumflex and right coronary artery lesions, but the left ventricular function remained normal. He remained asymptomatic at 1-year follow-up. His medications were modified to increase the dose of statins, add sirolimus, a proliferation signal inhibitor, and dual antiplatelet therapy to prevent subacute stent thrombosis. The parents were counseled about the need for a repeat cardiac transplantation whenever a deterioration of left ventricular function is detected. According to the advice of immunologists, titrated doses of tacrolimus, mycophenolate mofetil, and prednisolone were continued.

DISCUSSION

An initial immunological injury to the graft endothelium due to multiple donor and recipient factors leads to altered endothelial permeability and subsequent intimal hyperplasia.^[1] Subsequent nonimmunological factors such as ischemia reperfusion, viral infections, and atherosclerotic risk factors perpetuated by

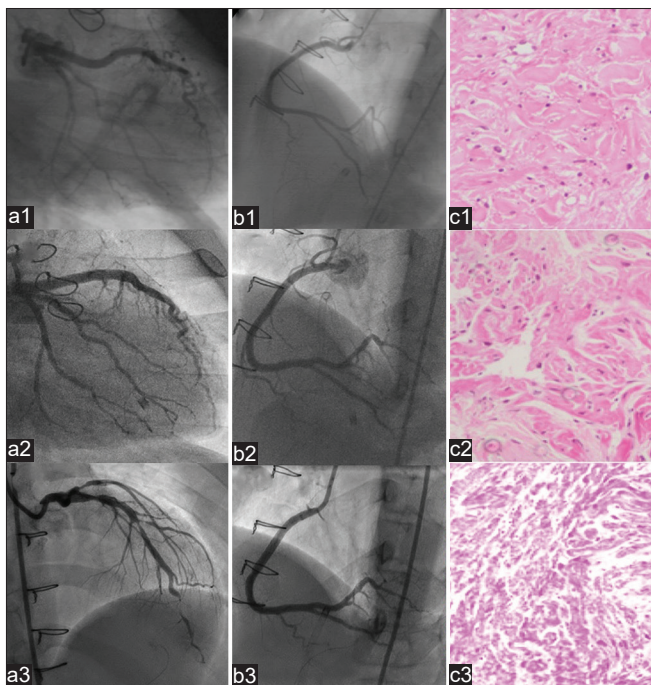


Figure 1: Serial left (a) and right (b) coronary angiography and endomyocardial biopsy (c) in the years 2015 (1), 2017 (2) and 2018 (3) are depicted here. The angiograms failed to show any luminal narrowing till 2017, but there was severe proximal, mid and distal left anterior descending coronary artery stenosis in 2018. There was no evidence of rejection in the biopsy

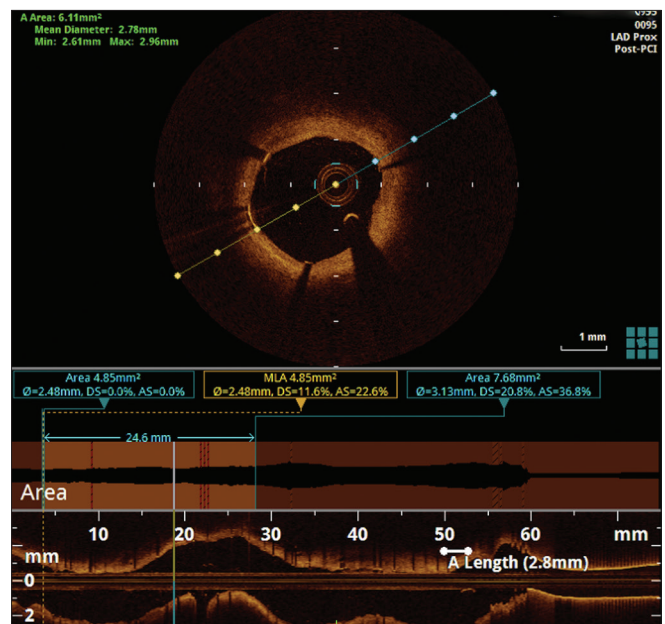


Figure 2: Optimal coherence tomography showing severe diffuse intimal hyperplasia more than 0.5 mm in the entire right coronary artery shown on cross sections and pull-back M mode view

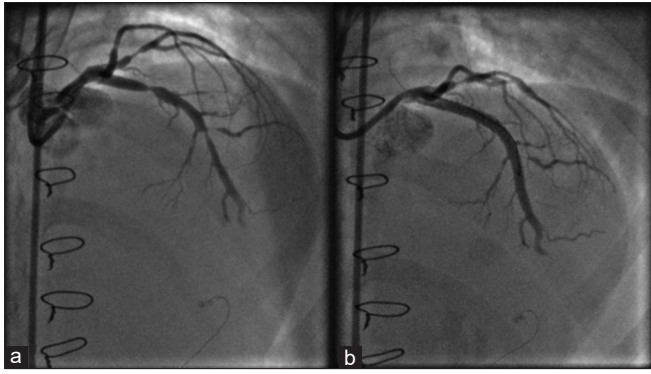


Figure 3: Following stent angioplasty of the proximal and mid left anterior descending coronary artery with a very long stent, the lumen appears wide open with thrombolysis in myocardial infarction 3 flows

immunosuppressive drugs continue the endothelial injury.^[5] As CAV is associated with graft loss and mortality, primary prevention of hypertension, hyperglycemia, and hyperlipidemia and viral prophylaxis are introduced early. Ongoing research targets genetic modulators and inflammatory cytokines.^[6]

The traditional detection of CAV with coronary angiography is invasive, expensive, exposes to radiation, and fails to identify early disease. The sensitivity improves with the newer imaging using IVUS and OCT, which remain technically challenging due to the nonavailability of coronary guide catheter curved to suit a small pediatric patient.^[4] Noninvasive technology with stress echocardiography, strain imaging, tissue Doppler imaging, contrast echocardiography, cardiac magnetic resonance, nuclear perfusion imaging, and multislice computed tomography may give clues to the diagnosis prior to invasive imaging. Percutaneous coronary intervention in CAV is characterized by good short-term results, and the high restenosis rates are marginally reduced with the use of drug-eluting stents.^[7] Surgical revascularization also has limited success and is associated with a very high mortality up to 40%.^[8] Even though retransplantation is the only definitive treatment, it is associated with lower survival than with the primary graft and a recurrence of CAV of 50% at 3 years.^[9]

Our patient with rapidly progressive CAV had a temporary respite following a stent angioplasty. On a detailed literature search, we did not come across a report of percutaneous coronary intervention for CAV in pediatric age in the Indian subcontinent. A close echocardiographic follow-up is planned for assessing left ventricular function to decide about the timing of the repeat cardiac transplantation, which remains the only definitive management. In the presence of normal left ventricular function, natural history of CAV after drug-eluting stents seems similar to a repeat transplantation.^[10]

As an initial endothelial immunological injury triggers the onset of CAV, a pretransplant identification of panel-reactive antibodies or donor-specific single-bead antibodies is managed with plasmapheresis, intravenous gammaglobulins, and/or monoclonal antibodies. Once CAV is diagnosed, strategies include increasing statins for their pleiotropic activity, commencing dual antiplatelet therapy, supplementing proliferation signal inhibitors such as sirolimus or everolimus, counseling and listing for a repeat cardiac transplantation, and close serial echocardiographic follow-up for deteriorating left ventricular function to finalize the timing of the next transplantation.^[10]

CONCLUSION

CAV presents challenges in diagnosis due to lack of warning signs and is diagnosed by coronary angiography and advanced imaging. Drug-eluting stent angioplasty offers a less invasive alternative to surgical bypass and retransplantation and works best in patients who have critical localized disease instead of diffuse triple-vessel disease. The progress of vascular disease is more accelerated than atherosclerosis. Our first report of a successful percutaneous intervention in CAV in the Indian subcontinent serves as an eye-opener to meticulously look for this complication following transplant by serial angiographies or advanced imaging.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names 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.

REFERENCES

1. Pahl E, Naftel DC, Kuhn MA, Shaddy RE, Morrow WR, Canter CE, *et al.* The impact and outcome of transplant coronary artery disease in a pediatric population: A 9-year multi-institutional study. *J Heart Lung Transplant* 2005;24:645-51.
2. Rahmani M, Cruz RP, Granville DJ, McManus BM. Allograft vasculopathy versus atherosclerosis. *Circ Res* 2006;99:801-15.
3. Kobayashi D, Du W, L'ecuyer TJ. Predictors of cardiac allograft vasculopathy in pediatric heart transplant

- recipients. *Pediatr Transplant* 2013;17:436-40.
4. Cassar A, Matsuo Y, Herrmann J, Li J, Lennon RJ, Gulati R, *et al.* Coronary atherosclerosis with vulnerable plaque and complicated lesions in transplant recipients: New insight into cardiac allograft vasculopathy by optical coherence tomography. *Eur Heart J* 2013;34:2610-7.
 5. Dedieu N, Greil G, Wong J, Fenton M, Burch M, Hussain T. Diagnosis and management of coronary allograft vasculopathy in children and adolescents. *World J Transplant* 2014;4:276-93.
 6. Schumacher KR, Gajarski RJ, Urschel S. Pediatric coronary allograft vasculopathy – A review of pathogenesis and risk factors. *Congenit Heart Dis* 2012;7:312-23.
 7. Lee MS, Yang T, Kandzari D, Mahmud E, Liao H, Kirtane A. Long-term clinical outcomes in patients treated with drug-eluting compared to bare-metal stents for the treatment of transplant coronary artery disease. *Catheter Cardiovasc Interv* 2012;80:533-8.
 8. Halle AA 3rd, DiSciascio G, Massin EK, Wilson RF, Johnson MR, Sullivan HJ, *et al.* Coronary angioplasty, atherectomy and bypass surgery in cardiac transplant recipients. *J Am Coll Cardiol* 1995;26:120-8.
 9. Topkara VK, Dang NC, John R, Cheema FH, Barbato R, Cavallo M, *et al.* A decade experience of cardiac retransplantation in adult recipients. *J Heart Lung Transplant* 2005;24:1745-50.
 10. Goldraich LA, Stehlik J, Kucheryavaya AY, Edwards LB, Ross HJ. Retransplant and medical therapy for cardiac allograft vasculopathy: International society for heart and lung transplantation registry analysis. *Am J Transplant* 2016;16:301-9.