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EDITOR'S NOTE

Dr Manoj Durairaj

Heart Transplant Surgeon, MS, MCh. (AIIMS, New Delhi), FACC.

Director, Marian Cardiac Centre and Research Foundation.

Program Director, Department of Heart and Lung Transplantation, Sahyadri Hospitals, Pune.

Dear Readers,

Greetings. In this issue Dr Madhu Sankar our guest author highlights the long-term results of heart transplants with 2 index case illustrations. The first patient had a coronary allograft vasculopathy after 8 years which necessitated an urgent VA ECMO insertion in 2017 and a Balloon Atrial Septostomy to decompress the left heart. She underwent a Redo Heart Transplant under supra urgent category and is doing well 6 years post Redo Heart Transplant. The long-term survival rates post heart transplant are 21% at 20 years which establishes this modality as a Gold Standard therapy for End Stage Heart Failure.

Wishing all our dear Readers a Happy Reading!

Dr Manoj Durairaj
Editor "The Revival"

SUB EDITOR

Dr Talha Meeran

MBBS, MD, FACC, Consultant Cardiologist, Dept of Advanced Cardiac Sciences and Cardiac Transplant, Sir HN Reliance Foundation Hospital, Mumbai.

Dear Colleagues,

Coronary allograft vasculopathy is considered the Achilles heal for long term survivorship post cardiac transplant and can present in varying severities. This edition of REVIVAL highlights two cases of cardiac transplant beyond 10 yrs of their transplants. The first case demonstrates how severe CAV could in rare instances present as acute cardiogenic shock. Timely interventions with ECMO and atrial septostomy helped in stabilizing this patient and eventually bridging to a successful re-do cardiac transplant. The second case highlights a cardiac transplant case with no CAV and consequently un-eventful long term post transplant course.

Sincerely,
Dr Talha Meeran
Sub Editor "The Revival"

PRESIDENTIAL MESSAGE

Prof. (Dr) V. Nandakumar

Director & Chief, Division of Cardio Vascular/Thoracic Surgery & Cardiac Transplantation, Metromed International Cardiac Centre, Calicut, Kerala.

Dear Colleagues,

In this February issue of 'The Revival' Dr Madhu Sankar presents two interesting cases of cardiac transplantation with good long term results. It is quite encouraging to see how a person with extensive cardiac allograft vasculopathy presenting in cardiogenic shock can be saved with drastic measures and retransplantation with long lasting results. Dr Madhu Sankar has briefly discussed various postoperative long term problems associated with cardiac transplantation especially the role of cardiac allograft vasculopathy. At the same time in the second case even after 7 years post transplant, he had normal coronaries with cyclosporine and mycophenolate, which is quite promising.

Best wishes,
Prof. (Dr) V. Nandakumar
President

Please call or write to us:
Call: 9822322072, 9167048815,
manojdurairaj@hotmail.com,
talha.meeran@gmail.com

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Special thanks to Dr N. Madhu Sankar and Dr KM Cherian for authoring this month's article.

Designed by Maithili Kulkarni

LONG TERM SURVIVAL AFTER HEART TRANSPLANT

DR N MADHU SANKAR
M.S., PhD, DNB, (CTVS)

Sr. Cardiothoracic Surgeon and Heart and Lung Transplant Surgeon. Sree Mookombika Institute of Medical Sciences, Kulasekharam, K K Dt, TN.

Qualification:

MBBS from Tirunelveli Medical College -1984

M.S (Gen. Surgery) from Tirunelveli Medical College -1987

Ph.D ., in Cardiovascular surgery from National Research Centre of Surgery, Academy of Medical Sciences, Moscow, USSR -1990

DNB – Cardiothoracic Surgery, National Board of Examinations – New Delhi.

Areas of Specialisation:

- Coronary Bypass surgery
- Valve Repair and Replacement Surgery, Surgery for Atrial Fibrillation
- Heart and Lung Transplantation

Awards and Achievements :

- Fellowship in Heart and Lung Transplantation from St Vincents Hospital, Sydney – 1996.
- Cardiac Surgery Specialist Fellowship (1 Year) at Westmead Hospital, Sydney -1997.
- Life Member and fellow of Indian Association of Cardiothoracic Surgery.
- Executive Member of Indian society of Heart Failure
- Involved in Transmyocardial Laser Revascularization Project
- Actively involved in Heart & Lung Transplantation and Stem Cell Therapy
- First in the country to transport Donor Heart in commercial airline and perform Heart Transplantation
- Has more than 60 publications in cardiac surgery in **International Journals.**
- Appointed as **Adjunct Professor** of The Tamilnadu DR M G R Medical University from Dec 2011.
- Performed **the first successful single lung transplant** in INDIA in Dec 2011

DR KM CHERIAN
MS., FRACS

Frontier Lifeline Hospital, Chennai.

He is the founder of Frontier Lifeline Hospital, where he performed India's second heart transplant surgery in 1995. He also performed the country's first heart-lung transplant and the country's first pediatric cardiac surgery.

Awards and honours :-

- He was awarded **Padma Shri** by the Government of India in 1991, and was honorary surgeon to the President of India from 1990 to 1993.
- In June 2000, Dr Cherian received **a lifetime achievement award from Kasturba Medical College** for contributions made to the field of cardiothoracic surgery in India.
- He received a **Harvard Medical Excellence Award in 2005**, through a panel organised by Harvard Medical School.
- His name is engraved in one of the stones at Kos Island, Greece along with three other Indian surgeons, on the occasion of the 18th World Congress held by the World Society of Cardio Thoracic Surgeons held between 30 April – 3 May 2008.
- In 2010, Cherian became the first Indian to be designated president of the World Society of Cardio Thoracic Surgeons.
- In May 2016, Cherian was selected to be a member of the **"Founder Circle"** of the American Association for Thoracic Surgery.

INTRODUCTION:

Heart transplant is the gold standard in treatment of patients with end stage heart disease. The one year survival is nearly 90 % and five year survival is 80% in established centers. There is significant improvement, compared to the 1 year and 5 year survival rate of 1980s. As per the International Registry ,21 % of patients are alive after 20 years. Even higher results have been reported from experienced centers. The longterm outcome is influenced by the development of coronary allograft vasculopathy and occurrence of malignancies.

Case 1:

A 36 years old lady Ms. R , was diagnosed with dilated cardiomyopathy and stage IV heart failure. She was evaluated for heart transplant and underwent orthotopic heart transplant in 2009 and was on regular follow up. She represented India in Transplant Olympics in 2017 in 100 meters in Barcelona. In May 2017, her echo showed mild RV dysfunction with good LV function. Coronary angiography revealed Cardiac allograft vasculopathy, affecting all 3 coronaries. RV endomyocardial biopsy showed no evidence of rejection. In September 2017, she presented to the emergency department in cardiogenic shock. The lactate levels were high with borderline hemodynamics. Intraaortic balloon Pump was inserted and resuscitated. A few hours later percutaneous femoro femoral V A ECMO was inserted. The hemodynamics was stabilized. Coronary angiography was done, which showed severe progression of CAV, severe biventricular dysfunction with significantly elevated NT Pro-BNP levels. Endomyocardial biopsy revealed grade I rejection. The next day she underwent Balloon Atrial Septostomy for left heart decompression.(Fig 1 and 2). Under supra urgent category, matching blood group donor was available on the third day, and she underwent successful redo heart transplant. She was discharged on 12th postop day. Prior to discharge, EMB showed no evidence of rejection and circulating cell free DNA levels were satisfactory. She is on regular follow up and doing well at 5 years, after redo heart transplant.

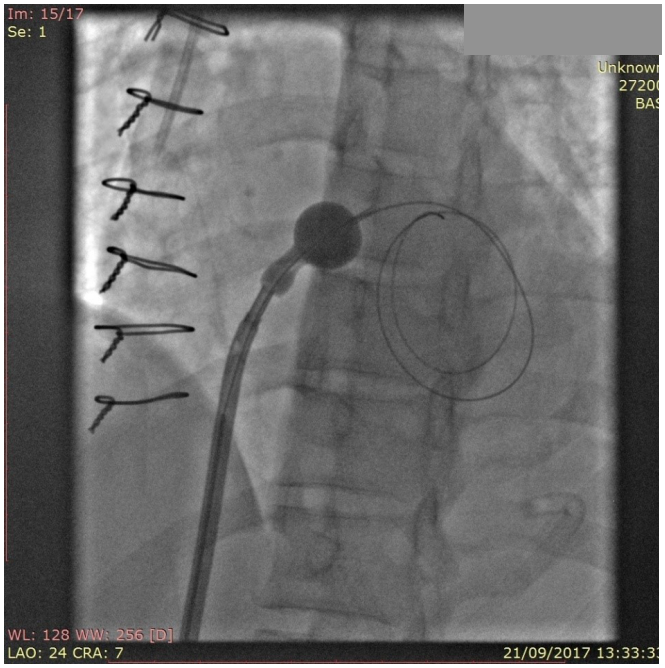

Fig 1: Before Balloon Atrial septostomy

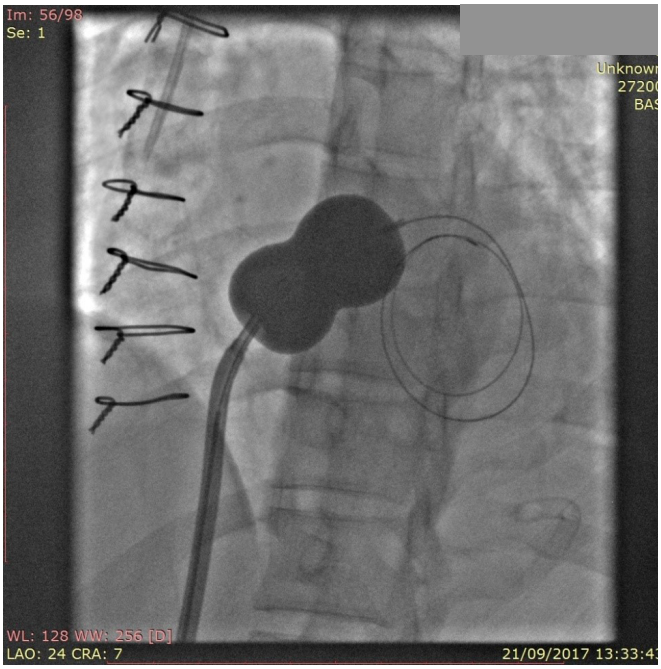

Fig 2.: After inflation of balloon

Case 2:

Mr. M, 50 yrs old gentleman from Chennai presented to us with Class IV dyspnea, dilated cardiomyopathy and severe LV dysfunction. His coronary angiogram revealed normal coronaries. He was evaluated for heart transplant. He underwent orthotopic heart transplant on 5.9.2009, from an in house donor. The total CPB time was 105 minutes and the cold ischemic time was 29 minutes. He is receiving triple drug immunosuppressive therapy and on regular follow up. Currently he is receiving 50 mg cyclosporine twice a day, Tab Myforetic 360 mg in the morning and 180 mg in the evening, Tab. Amlodipine 5 mg in the morning and Atorvastatin 20 mg in the evening. In September 2016, he had coronary angiogram , which showed normal coronaries. He is on regular follow up with 2D Echocardiography and blood investigations once in 3 months.

DISCUSSION:

Nearly 90% of patients who undergo heart transplant live for at least 1 year after the surgery. The risk of death is highest in the first year and the common causes are failure of the graft, rejection of the organ and infectious complications. After 5 years, malignancies and cardiac allograft vasculopathies are causes of mortality. Immunosuppressed allograft recipients have 3 to 5 fold increase in cancer risk as compared age matched general population. The most common malignancies encountered are non melanotic skin cancer, post transplant lymphoproliferative disorder and kaposi's sarcoma. Duration of immunosuppressive therapy and / or type of immunosuppressive agents are important controllable factors which have an impact in the development of tumors. Oncogenic viruses have an important role in the development of these malignancies.

Post-transplant lymphoproliferative disorders (PTLD) occurs in 2 – 6 % of cardiac transplant recipients. The peak occurrence of PTLD is 3 – 4 months after transplantation. The initial management of PTLD involves reducing the amount of immunosuppression. Non-responding patients may require aggressive combination chemotherapy, but the mortality rate is approximately 80% in this situation.

Currently, women represent less than 25% of heart transplant recipients; this has been attributed to selection and referral bias and potentially poorer outcomes in female recipients. In a larger study, Moayadi, et al., compared survival outcomes after heart transplantation between males and females (11). When male and female recipients were matched for recipient and donor characteristics, there were no significant survival differences.

Cardiac allograft vasculopathy is manifested by unusually accelerated form of coronary disease affecting both intramural and epicardial coronary arteries . Intracoronary ultrasound studies have shown that non circumferential plaques in proximal segments and sometimes diffuse concentric pattern in distal segments. In a multi institutional study ,the actuarial likelihood of any angiographically visible CAV is 11%, 22% and 45% at 1, 2 and 4 years respectively. Several non immunologic mechanisms could contribute to the progression of CAV .The recipient factors incriminated are age , sex, obesity , hypertension, hyperlipidemia , insulin resistance and CMV infection . The donor characteristics incriminated are age, sex, pre-existing coronary artery disease and donor ischemic time.

Repeat cardiac transplantation has been performed, but survival after retransplantation is shorter than after the initial transplantation. Redo heart transplantations are indicated in 3 distinct situations: (1)Primary graft dysfunction (2) Acute / chronic rejection manifesting as allograft dysfunction(3) Coronary allograft vasculopathy presenting with failure.

The best results are those with redo heart transplant, despite the fact that majority of them have renal dysfunction and may require combined heart kidney transplantation.

UNOS registry has analysed the total of 40,711 recipients including 39,657 (97.4%) primary and 1054(2.6%) redo heart transplant. 1 and 5 year survivals were lower after redo orthotopic heart transplant. Contingent on 1 year survival ,donor factors such as hypertension and Left ventricular ejection fraction < 50% negatively affected survival at 5 years (6)

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PRESIDENT

DR V NANDAKUMAR
Mob: 9843015888
Email: drvnandakumar@gmail.com

PRESIDENT ELECT

DR RONY MATHEW
Mob: 9846097812
Email: drronymathew@yahoo.com

VICE PRESIDENTS

DR JULIUS PUNNEN
Mob: 9980072785
Email: jpunnen@hotmail.com

DR AJITKUMAR V K
Mob: 9895153684
Email: ajitkumarvk@yahoo.com

SECRETARY

DR JABIR ABDULLAKUTTY
Mob: 9447011773
Email: drjabi@yahoo.co.in

JOINT SECRETARY

DR RAJAGOPAL S
Mob: 9747606600
Email: srajagovindam@gmail.com

TREASURER

DR PRAVEEN G PAI
Mob: 9847334434
Email: praveen.pai.g@gmail.com

PAST PRESIDENTS

DR GEEVAR ZACHARIAH
(2013-2014 and 2014-2015)
Mob: 9846066816
Email: geevarzachariah@gmail.com

DR SHIV K NAIR (2015-2016)
Mob: 9846010220
Email: Shivnairmd@gmail.com

DR K VENUGOPAL (2016-2017)
Mob: 9847005444
Email: venugopalknair@gmail.com

DR JOSE CHACKO PERIAPURAM (2017-2018)
Mob: 9847043224
Email: joseperiapuram@hotmail.com

DR P P MOHANAN (2018-2019)
Mob: 9846076006
Email: drppmohanan@yahoo.com

MEMBERS

DR C G BAHULEYAN
Mob: 9447344882
Email: bahuleyan2001@yahoo.co.uk

DR P CHANDRASEKHAR
Mob: 9443047152
Email: chanpad@gmail.com

DR COL JAMES THOMAS
Mob: 9892797060
Email: thomasdrjames@yahoo.in

DR JACOB ABRAHAM
Mob: 9847128123
Email: jacabraham1@gmail.com

DR JAYAGOPAL P B
Mob: 9847023777
Email: jaigopallakshmi@gmail.com

DR KARTHIK VASUDEVAN
Mob: 9845281450
Email: karvasudevan@gmail.com

DR C S HIREMATH
Mob: 9481119646
Email: hiremath.cs@sss.hms.org.in

DR MANOJ DURAIRAJ
Mob: 9822322072
Email: manojdurairaj@hotmail.com

DR RAJESH RAMANKUTTY
Mob: 9846005737
Email: drrajesh_mr@yahoo.com

DR V K CHOPRA
Mob: 9560898900
Email: chopravk@gmail.com

DR TALHA MEERAN
Mob: 9167048815
Email: talha.meeran@gmail.com