Giant Cell Myocarditis Patients Undergoing Heart Transplantation Have High Rates of Rejection, Infection and Cardiac Allograft Vasculopathy: Case Series

Heidi S. Lumish, Kevin J. Clerkin, Charles Marboe, Jiho Han, Farhana Latif, Susan W. Restaino, Maryjane A. Farr, Edward F. Lin, Hiroo Takayama, Koji Takeda, Yoshifumi Naka, Paolo C. Colombo, Melana Yuzefpolskaya [1]

[1] Columbia University Medical Center, New York City, USA

Introduction

- Giant cell myocarditis (GCM) is a rare often fatal autoimmune disease that affects young patients.
- Most patients are treated with immunosuppressive drugs.[1] However, survival is <10% at 5 years without the use of advanced therapies such as mechanical circulatory support (MCS) and/or heart transplantation (HT).[1]
- Following HT, high rates of rejection and recurrence of GCM have been observed in this population.[2-4]
- Infectious complications are seen in as high as 80% of patients post-transplant.[4]
- Therefore, optimal intensity of immunosuppression remains to be determined given high rates of rejections and infections.

Aims

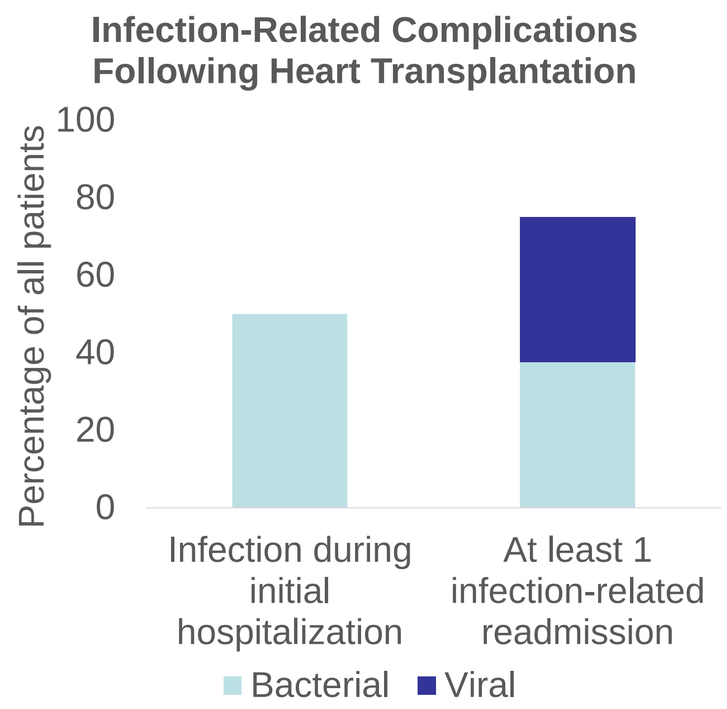
- **To describe rates of rejection and GCM recurrence in patients with giant cell myocarditis who have undergone HT at a large single institution**
- **To describe rates and types of infection in a series of patients with giant cell myocarditis following HT**

Methods

- Retrospective review of 845 patients who underwent heart transplantation at Columbia University Medical Center between January 1990 and June 2017 was performed.
- Eight patients with biopsy-proven giant cell myocarditis were identified, as reviewed by an independent pathologist (C.M.), and make up the final cohort as presented.

Results

- **Demographics**: The median age of the cohort was 44 years (IQR 30, 51). 62.5% of patients were female, 37.5% had pre-existing autoimmune disease, and 75% were blood type A.
- **Presenting symptoms**: The main presenting symptom was cardiogenic shock (50%), followed by cardiac arrhythmia (37.5%), and complete heart block preceding cardiogenic shock (12.5%).
- **Mechanical circulatory support**: Majority of patients required mechanical circulatory support with uni- or biventricular devices (62.5%) prior to HT. The remainder of patients were supported with inotropic therapy.
- **Rejection post-HT**: 75% of patient had rejection requiring treatment (Table). 83% of those with rejection had evidence of severe rejection (>= ISHLT 2R/3A). Median time to first rejection was 0.5 months (IQR 0, 2.5). All patients maintained their graft function at the end of follow-up.
- **CAV**: High rate of coronary allograft vasculopathy (CAV) was observed: 37.5% had ISHLT 1 CAV, 12.5% had ISHLT 2 CAV. Median time to CAV diagnosis was 6 years.
- **GCM recurrence**: Recurrence of GCM diagnosis was observed in 25% of patients. All treated cyclophosphamide alone or cyclophosphamide with steroids, in addition to their baseline immunosuppressive therapy. All patients cleared their infiltrate post-treatment.
- **Infection-related complications**: 50% had infection-related complications during their index hospitalization and 75% had at least one infection-related readmission



Case	Age	Sex	Follow-up duration (years)	Immunosuppressive regimen for GCM prior to HT	Time to first rejection (months)	Number of rejections (highest grade)	CAV	Immunosuppression			Recurrent GCM	Survival
								Induction	<1 year	Most recent follow-up		
1	54	F	1	Cyclosporine, steroids	N/A	0	N/A	None	Tacrolimus, MMF, steroids	Tacrolimus, steroids	N	Y
2	61	M	5	Cyclophosphamide, IVIG, steroids	N/A	0	1	None	Tacrolimus, MMF, steroids	Tacrolimus, everolimus, steroids	N	Y
3	32	F	7	Cyclophosphamide, steroids	3	2 (2R/3A)	0	Daclizumab	Tacrolimus, MMF, steroids	Tacrolimus, MMF, steroids	N	Y
4	50	M	9	Steroids	<1	1 (1R/1B)	0	Daclizumab	Cyclosporine, MMF, steroids	Cyclosporine, MMF, steroids	Y	Y
5	22	M	15	Cyclophosphamide, steroids	<1	3 (2R/3A)	1	OKT3	Tacrolimus, MMF, steroids	Tacrolimus, MMF, steroids	N	Y
6	37	F	5	Steroids	3	1 (2R/3A)	1	OKT3	Cyclosporine, MMF, steroids	Cyclosporine, steroids	Y	Y
7	50	F	17	Cyclophosphamide, hydroxychloroquine, steroids	0	7 (2R/3A)	0	None	Cyclosporine→ tacrolimus, MMF, steroids	Tacrolimus, steroids	N	Y
8	22	F	17	Cyclosporine, azathioprine, steroids	1	1 (2R/3A)	2	OKT3	Cyclosporine, steroids	Tacrolimus, steroids	N	N

GCM = giant cell myocarditis, HT = heart transplantation, CAV = cardiac allograft vasculopathy, MMF = mycophenolate mofetil, OKT3 = Muromonab-CD3

Conclusions

- **Patients with GCM who require HT have elevated risk of graft rejection (75% at 1 year), CAV (50% at 6 years post-HT), and infection (75% with infection requiring hospitalization).** [5]
- **Nevertheless, survival in this series is above the national average, with 100% 1-year and 5-year survival.**
- **Multicenter studies are needed to further characterize outcomes in this unique population.**

References

1. Ekstrom, K., et al. (2016). Long-term outcome and its predictors in giant cell myocarditis. *Eur J Heart Fail* **18**(12): 1452-1458.

2. Murray, L. K., et al. (2012). Ventricular assist device support as a bridge to heart transplantation in patients with giant cell myocarditis. *Eur J Heart Fail* **14**(3): 312-318.

3. Elamm, C. A., et al. (2017). Heart Transplantation in Giant Cell Myocarditis: Analysis of the United Network for Organ Sharing Registry. *J Card Fail* **23**(7): 566-569.

4. Montero S, Aissaoui N, Tadie JM, et al. (2018). Fulminant giant-cell myocarditis on mechanical circulatory support: Management and outcomes of a French multicentre cohort. *Int J Cardiol* 253: 105-112.

5. Lund, L. H., et al. (2017). The Registry of the International Society for Heart and Lung Transplantation: Thirty-fourth Adult Heart Transplantation Report-2017; Focus Theme: Allograft ischemic time. *J Heart Lung Transplant* **36**(10): 1037-1046.

Disclosures

This work was supported by **Lisa and Mark Schwartz Program to Reverse Heart Failure** at Columbia University Irving Medical Center.