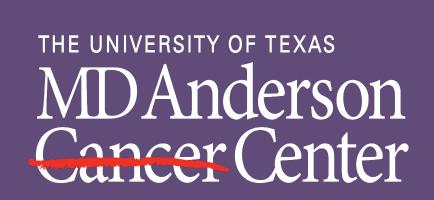# Immune Checkpoint Inhibitor Myocarditis: Concomitant Coronary Artery Disease and Heart Failure

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Background

- Despite promising cancer results from immune checkpoint inhibitors (ICI) several immune related adverse events (irAE) have been observed, including myocarditis.

- Though it has a low incidence, 0.5 to 1%, ICI myocarditis is the most fatal irAE with a reported mortality of 25 to 50%.

- ICI myocarditis diagnosis depends on a combination of clinical presentation: biomarkers, cardiac imaging, and endomyocardial biopsy.

- The clinical presentation of myocarditis is often equated with heart failure despite most patients presenting with normal left ventricular ejection fraction (LVEF).

- Current practice guidelines suggest to first rule coronary artery disease (CAD) prior to making a diagnosis of myocarditis.

Objective

To establish that the presentation of heart failure may not always indicate ICI myocarditis.

Methods

- A single center retrospective cohort study of all patients who had endomyocardial biopsy for suspected ICI myocarditis between January 2018 and January 2020 was performed.

- Manual electronic medical record review was performed to collect demographics, oncologic history, laboratory values, catheterization data, and cardiac imaging data.
  - Pulmonary capillary wedge pressure (PWCP) ≥12mmHg indicates heart failure and PCWP<12mmHg indicates no heart failure.

- Clinical parameters and right heart hemodynamics were compared using Chi-square test.

Results

- 52 patients had endomyocardial biopsy for suspicion of ICI myocarditis.
  - The mean age was 68 years and the majority were male (75%).
  - 42 (81%) patients had definite, probable, or possible myocarditis and the remaining were considered negative for myocarditis.

Table 1-Baseline Demographics

Demographics & Clinical Parameters Range	Definite Myocarditis n=26	Probable Myocarditis n=7	Possible Myocarditis n=9	Negative for Myocarditis n=11	P-value
Age, Median (IQR)	74 (66-77)	62 (58-73)	65 (63-69)	69 (66-76)	0.54
Gender % (M/F)	73/27	71/29	89/11	73/27	0.79
Race %					
White	73	57	67	27	0.4
Black	8	14	0	0	
Other	21	28	32	73	

Table 2-Right and Left Heart Catheterization Data at Time of Biopsy

Right/Left Heart Catheterization Data Median (IQR) Range	Definite Myocarditis n=26	Probable Myocarditis n=7	Possible Myocarditis n=9	Negative for Myocarditis n=11	P-value
Right atrial mean pressure	9 (7-11)	7 (4-9) 0-10	5 (5-12) 0-21	8 (8-9) 44271	0.44
Pulmonary artery systolic pressure	32 (26-36) 19-46	26 (25 -36) 21-57	35 (28-43) 24-58	33 (29-40) 23-54	0.6
Pulmonary artery mean pressure	20 (18-24) 13455	22 (14-24) 14946	27 (17-32) 13-42	22 (19-29) 15-35	0.65
Pulmonary capillary wedge pressure mean	12 (9-15) 44278	11 (8-13) 44313	16 (7-22) 12479	13 (10-16) 44461	0.79
Left ventricular end-diastolic pressure	20 (12-22) 12451	17 (14-19) 11810	22 (11-26) 12236	18 (15-19) 14-20	0.75
Cardiac index- Fick L/min/m2	2.8 (2.2-3.1) 1.4-3.8	2.3 (2.1-2.4) 2.1-2.5	2.1 (1.8-2.2) 1.3-2.3	3.1 (2.8-3.2) 2.2-3.3	0.07
Arterial aortic systolic blood pressure	128 (114-144) 88-169	138 (122-150) 102-154	114 (105-122) 89-163	128 (117-132) 114-164	0.37

- Of those with myocarditis, LVEF <50% was observed in 47% of patients and pulmonary capillary wedge pressure (PCWP) >12 mmHg was observed in 47% of patients
  - Elevated PCWP and LVEF <50% were not correlated (p=0.78).

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- 47% presented with dyspnea but presenting symptoms of dyspnea and elevated PCWP were not associated (p=0.09).

- Of the 8 patients presenting with dyspnea but with normal PCWP, 3 (38%) had concomitant myositis, myasthenia gravis, or guillian barre irAEs.

- Significant CAD was found on left heart cath in 26% of patients presenting with myocarditis but the presence of CAD was not associated with having elevated PCWP (p=0.14).

Conclusions

- ICI myocarditis has varied clinical presentations including heart failure

- Only half may actually have heart failure this may be present in those with both normal and depressed LVEF.

- With patients presenting with dyspnea but have normal filling pressures on echocardiogram, concomitant muscular/neuromuscular junction irAEs should be considered.

- Cancer and CAD have shared risk factors and up to a quarter of patients presenting with myocarditis may have concomitant CAD

- The presence of CAD should not rule out myocarditis.

References

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