Lack of Correlation Between Cardiac Magnetic Resonance Imaging and Endomyocardial biopsy in Immune Checkpoint Inhibitor-Associated Myocarditis

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Background

- Endomyocardial biopsy (EMB) is the current gold standard for diagnosis of immune checkpoint inhibitor (ICI) myocarditis
- EMB is invasive with risk of serious complications in <1% of cases
- Cardiac magnetic resonance imaging (CMR) is a non-invasive test that has established criteria for the diagnosis of myocarditis, with a high reported diagnostic accuracy in general myocarditis[1]
- The role of CMR compared to EMB for the detection of ICI-associated myocarditis has not been examined

Objective

- To examine the agreement between CMR and EMB in immune checkpoint inhibitor-associated myocarditis

Methods

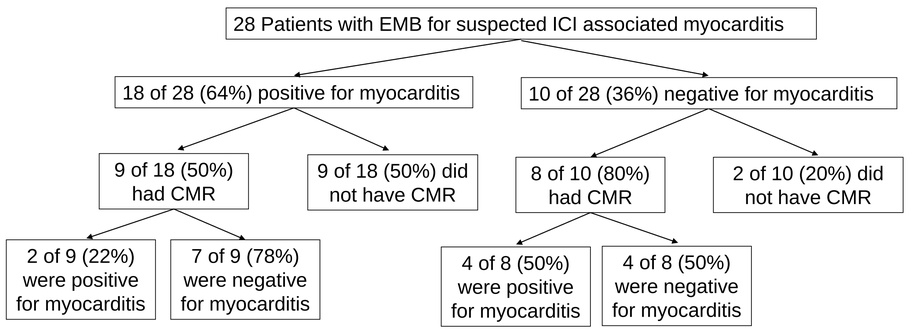
- Retrospective study evaluating all patients who had an EMB and were on or had received ICI between January 1, 2018 and May 31, 2010
- At our institution an EMB with 4 to 6 specimens is standard for patients with suspected ICI myocarditis
- Contraindications to EMB
  - Platelets <50,000, INR>2, lack of large vein access, clinically unstable, patient refusal
- Cardiac pathologists trained in heart transplant rejection reviewed all EMB for the diagnosis of myocarditis defined by inflammatory infiltrate[2]
- CMR images were acquired using a 1.5T MRI scanner GE AW (Milwaukee, WI)
- All CMR images were evaluated by a cardiologist board-certified in CMR. Myocarditis was evaluated using the Updated Lake Louise Criteria (2 out of 2) with supportive criteria[3]
- CMR that met 2 out of 2 main criteria or met 1 main criterion and had supporting evidence were recorded as positive for myocarditis

Results

Baseline Demographics and Cardiac Studies

Characteristic	EMB positive n= 18	EMB negative n=10	All Patients n=28
Sex- (%)			
Female	22	40	29
Male	78	60	71
Median age (range)- years	75 (24-95)	69 (41-87)	67 (24-95)
Race- (%)*			
White	78	70	75
Black	11	10	10
Other	11	20	16
Cancer types (%)			
Genitourinary	39	30	36
Melanoma	22	10	18
Head & Neck	22	10	18
Lung	11	10	7
Lymphoma	-	20	7
Other**	6	20	14
Comorbidities (%)			
Hypertension	67	80	71
Hyperlipidemia	39	40	39
Diabetes	33	10	25
Coronary Artery Disease	28	10	21
Peripheral Artery Disease	6	10	7
Stroke	6	10	7
Presenting EKG (%)			
Normal sinus rhythm	28	50	36
Sinus bradycardia	17	-	11
Sinus tachycardia	11	20	14
1st, 2nd, or 3rd degree AV block	11	10	11
Atrial fibrillation	11	10	11
RBBB or LBBB	22	10	18
Presenting LVEF (%)			
>50%	67	30	54
40-50%	22	10	18
<40%	11	60	29
Checkpoint blockade (%)			
CTLA-4 and PD1	28	10	21
PD1	67	70	68
PDL1	6	10	7
CTLA4	-	10	4

*Race was self-reported.** Other malignancies included Hepatocellular Carcinoma, Mucinous Appendiceal Adenocarcinoma, Endometrial cancer, Breast cancer, and Myelodysplastic syndrome

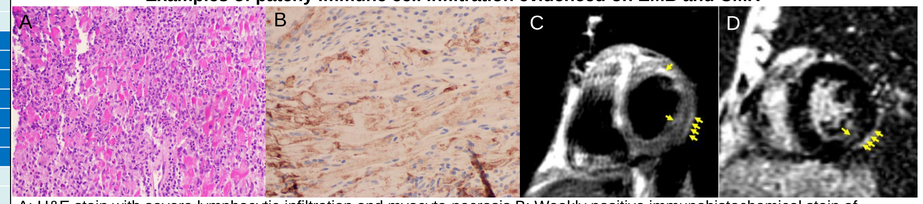


- EMB and CMR had 6/17 (35%; 90% CI: 17-58%) agreement

	EMB Positive	EMB Negative	Total
CMR Positive	2	4	6
CMR Negative	7	4	11
Total	9	8	17

- 18 (64%) patients had EMB positive for myocarditis and all had positive PDL1+ immunohistochemical staining
  - 7 of the positive EMB had inflammatory infiltrate and myocyte necrosis
  - 11 of the positive EMB had inflammatory infiltrate without necrosis meeting Marburg criteria for myocarditis[2]
- 17 (61%) patients also had CMR performed
  - 2 of the positive CMR met 2 out of 2 criteria
  - 4 of the positive CMR met 1 criteria and had supporting evidence of myocarditis
- The 4 patients with CMR positive for myocarditis and negative by EMB noted focal myocarditis in non-septal regions of the left ventricle

Examples of patchy immune cell infiltration evidenced on EMB and CMR



A: H&E stain with severe lymphocytic infiltration and myocyte necrosis B: Weakly positive immunohistochemical stain of PDL1 (22C3 Ab) C:T2 weighted imaging showing patchy myocardial edema and myocardial edema that correlates with some areas of late gadolinium enhancement in slide D. D:Late gadolinium enhancement image showing patchy epicardial enhancement at the inferolateral wall in a non-coronary artery disease distribution.

Conclusions

- The correlation of CMR and EMB in patients with ICI myocarditis appears lower than reported for myocarditis in general
- Patchy immune cell infiltration in ICI myocarditis may result in false negative EMB
- At present, clinicians should consider performing both CMR and EMB for evaluation of clinically suspected ICI myocarditis

References

1. Friedrich, M et al. Cardiovascular Magnetic Resonance in Myocarditis: A JACC White Paper. *J Am Coll Cardiol* 2009; 53(17):1475-1487.

2. Maisch B et al. World Heart Federation consensus conferences's definition of inflammatory cardiomyopathy (myocarditis): report from two expert committees on histology and viral cardiomyopathy. *Heartbeat* 1999;4:3–4.

3. Ferreira et al. 2018 Update of CMR Criteria for Myocardial Inflammation. *J Am Coll Cardiol* 2018; 72(24): 3158-76.

Disclosures

The authors have no relevant disclosures.