Corticosteroid Refractory Immune Checkpoint Inhibitor Myocarditis Treated with Infliximab

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INTRODUCTION

- The use of immune checkpoint inhibitors (ICI) in cancer management has significantly increased in recent years.
- Cardiovascular immune-related adverse events, particularly myocarditis, have been increasingly recognized.
- Beyond treatment with high dose steroids, there is a paucity of data of optimal therapy should steroids fail.
- We present a case series of steroid refractory ICI cardiac toxicity treated with infliximab.

METHODS

- In this study we retrospectively identified patients that had ICI myocarditis at a single large academic center.
- We sought to analyze patient characteristics and outcomes in those who had steroid refractory ICI myocarditis requiring treatment with infliximab.

STUDY POPULATION

Table 1: Demographics

Baseline Characteristics	N = 4
Age, years (mean ± SD)	61.75 ± 4.6
Female	2 (50%)
HTN	2 (50%)
DM	0 (0%)
Tobacco Use	0 (0%)
CAD	0 (0%)
HF	0 (0%)
CVA	0 (0%)
OSA	0 (0%)
CKD	1 (25%)
BMI (kg, m^2)	27.66 ± 9.8
Prior Anthracycline exposure	0 (0%)
Prior Radiation	1 (25%)
Hx of VEGF exposure	0 (0%)
Mean Follow-up Time (mean ± SD)	198 ± 147 days
Time from last ICI dose to onset of symptoms	38 ± 3.3 days

HTN = hypertension, DM = diabetes Mellitus, CAD = coronary artery disease, HF = heart failure, CVA = cerebral vascular disease, OSA = obstructive sleep apnea, CKD = chronic kidney disease, BMI = body mass index, VEGF = vascular endothelial growth factor

RESULTS

Table 2: Individual Patient Characteristics

	Malignancy	ICI received	Total ICI Doses	Cardiac Manifestation	Treatment
Patient 1	Ovarian Adenocarcinoma	Pembro-lizumab	2	CHF, VT	Solumedrol 1g x3, infliximab 5mg/kg
Patient 2	Metastatic RCC	Nivolumab	1	CHF, CHB, VT, Cardiogenic Shock	Solumedrol 1g x3, infliximab 5mg/kg
Patient 3	Metastatic Melanoma	Nivolumab	3	CHF, CHB, VT	Solumedrol 1g x3, infliximab 5mg/kg
Patient 4	Metastatic Melanoma	Nivolumab	9	CHF, VT Cardiogenic Shock	Solumedrol 1g x3, infliximab 5mg/kg

ICI: immune checkpoint inhibitor, CHF: congestive heart failure, VT: ventricular tachycardia, CHB: complete heart block.

FIgure 1: Clinical Course of Individiual patients

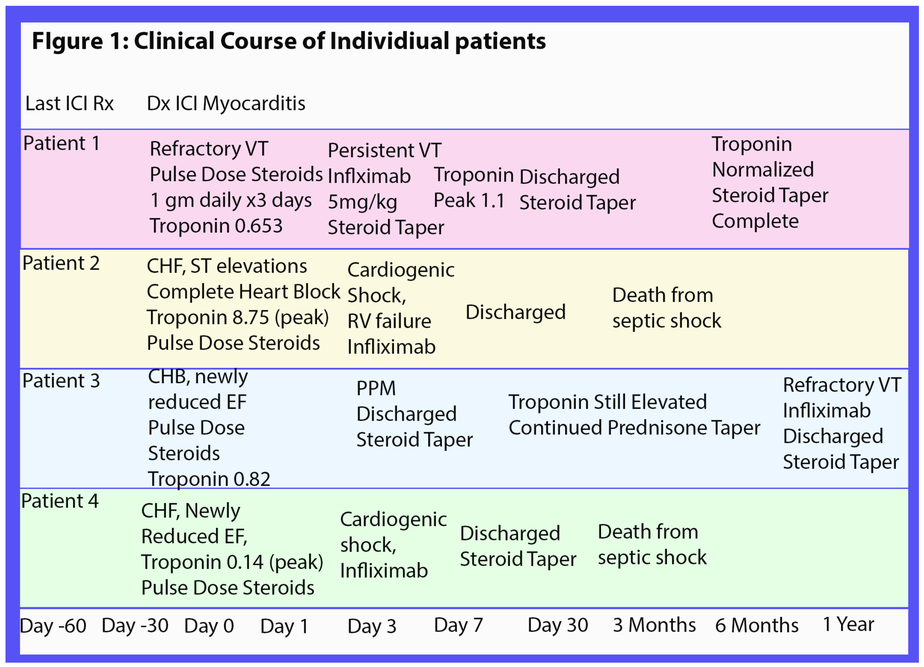

Table 3: Individual Patient Diagnostic Data

	Baseline EF (%)	Baseline LVIDD (cm)	EF (%) at dx	LVIDD (cm) at dx	Initial Troponin T (ng/ml)	Peak Troponin (ng/ml)	Time for troponin resolution (days)	Diagnostics
Patient 1	65%	3.92	35%	4.1	0.653	1.1	213	Negative LHC
Patient 2	60%	4.0	45%	3.8	8.75	8.75	62	Negative LHC, inconclusive biopsy
Patient 3	No prior echo		40%	4.8	0.82	0.82	378	Negative LHC
Patient 4	65%	5.1	35%	6.2	0.12	0.146	37	Negative LHC, LGE on MRI

EF: ejection fraction, LVIDD: left ventricular internal diameter in diastole, LHC: left heart catheterization, LGE: late gadolinium enhancement

CONCLUSIONS

- Infliximab has been successful in treating other ICI related adverse events such as colitis and pneumonitis but has been used sparingly in myocarditis due to its contraindication in heart failure.
- Our case series demonstrates cardiac safety in administration of infliximab in this patient population.
- Benefits of using infliximab as rescue therapy in steroid refractory ICI myocarditis may outweigh the risks.
- Additional studies are needed to evaluate efficacy and safety of infliximab in this population.

CLINICAL IMPLICATIONS

- Steroid refractory ICI myocarditis has a high mortality and in these patients we have demonstrated that infliximab can be a safe escalation immunosuppressive agent.

LIMITATIONS

- There was no control arm
- Sample size was small
- Retrospective
- Single center study

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