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Immune Checkpoint Inhibitor–Associated Myocarditis: A Retrospective Case Series

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Running Head title: ICI-Associated Myocarditis Case Series

What is new/ important

This manuscript explores a rare but serious complication of immune checkpoint inhibitor (ICI) therapy: myocarditis. We highlight the critical need for early recognition, thorough risk evaluation, and prompt treatment. In one notable case, myocarditis occurred alongside myasthenia gravis, adding complexity to both diagnosis and management. Our findings emphasize the value of a multidisciplinary approach. We also discuss how ASCO grading and tailored immunosuppressive strategies based on individual risk can support clinical decision-making and potentially improve outcomes for patients receiving ICI treatment.

Abstract

Background: Immune checkpoint inhibitors (ICIs) improve outcomes across malignancies but can cause immune-related adverse events (irAEs), notably myocarditis, with case-fatality up to 50%

Methods: We retrospectively reviewed five patients with potential ICI-associated myocarditis treated at Mayo Clinic Florida (2019–2024) and summarize the existing literature. Cases were retrospectively categorized as definite, probable, or possible myocarditis according to cardiac magnetic resonance (CMR) findings and histopathology when available.

Results: The median age was 74 years, and four of the five patients were male. Myocarditis developed between 5 and 30 days after initiation of anti–PD-1 therapy. Presentations included dyspnea (three patients), chest pain (one patient), and asymptomatic troponin elevation detected on routine monitoring (one patient). Troponin T elevation above the 99th percentile was seen in all five cases (normal <= 15 ng/L). Electrocardiograms (ECG) demonstrated conduction abnormalities or ventricular ectopy in each patient. Left ventricular ejection fraction was preserved in four patients and severely reduced in one.

CMR provided findings supportive of myocarditis in two of the five cases, while one endomyocardial biopsy (EMB) was performed and did not demonstrate active inflammation. Based on predefined criteria, one case was classified as definite myocarditis, one as probable, and three as possible ICI-associated myocarditis.

All five patients received corticosteroid therapy. Two required escalation of immunosuppression. One patient developed concurrent myasthenia gravis, consistent with myocarditis–myositis–myasthenia (MMM) overlap, and underwent plasmapheresis for the neuromuscular component. Three patients recovered. Two patients died during follow-up; in both cases, myocarditis was considered a contributing factor, although direct causality could not be definitively established.

Key words: Immune checkpoint inhibitors, myocarditis, Lake Louise criteria, ASCO grading

INTRODUCTION

Cancer remains the second most common cause of illness and death in the United States, with over two million new cases and more than 600,000 cancer-related deaths expected in 2024 [1]. In recent years, immune checkpoint inhibitors (ICIs) have significantly changed cancer treatment, improving survival rates across a range of cancers. Despite these advances, ICIs carry certain risks. By interfering with the body's natural immune regulation, they can lead to immune-related adverse events (irAEs). These events occur when activated T-cells mistakenly target healthy tissues, potentially triggering autoantibody production and the release of inflammatory cytokines [2].

Although irAEs most commonly affect the skin, gastrointestinal tract, endocrine organs, lungs, liver, and musculoskeletal system [3], cardiovascular complications, though less frequent can be particularly severe. Among them, myocarditis is one of the most dangerous, with an estimated incidence of 0.04% to 1.14% and a mortality rate approaching 60% in some

cases [4,5]. An especially concerning manifestation involves an overlap syndrome that includes myocarditis, myositis, and myasthenia gravis (MMM). Though rare, this condition has been associated with rapid clinical deterioration and early mortality [6].

We present five cases of suspected ICI-associated myocarditis encountered at our institution and explore current literature to better understand its diagnosis, management, and implications for clinical practice.

MATERIALS AND METHODS

We conducted a retrospective case series at Mayo Clinic Florida, reviewing patients treated between January 2019 and December 2024. Eligible participants had received at least one FDA-approved immune checkpoint inhibitor (ICI) and were clinically suspected of myocarditis. Cases were categorized based on degree of diagnostic confirmation. “Definite myocarditis” required fulfillment of revised 2018 Lake Louise CMR criteria [7] or histopathologic confirmation by endomyocardial biopsy. “Probable myocarditis” was defined as elevated cardiac biomarkers with supportive but non-diagnostic imaging and strong clinical context. “Possible myocarditis” was defined as biomarker elevation with compatible clinical features but limited or absent confirmatory imaging.

CMR scans were assessed according to the revised 2018 Lake Louise criteria, which require at least one marker of edema (T2-based) and one marker of tissue injury (T1-based) to support the diagnosis [7]. For cases where endomyocardial biopsy (EMB) was performed, interpretations adhered to established consensus criteria for myocarditis, while acknowledging the known limitations of myocardial tissue sampling [8]. Data related to clinical progression, immunosuppressive treatment strategies, and patient outcomes were extracted from electronic health records and reviewed manually by the study team.

RESULTS

A total of five patients had potentially developed myocarditis following treatment with anti–PD-1 immune checkpoint inhibitors (nivolumab or pembrolizumab). The median age was 74 years, and four of the five were male. On average, myocarditis onset occurred 23 days after the first ICI dose, with a range of 5 to 30 days. The patients had a variety of underlying malignancies: two had renal cell carcinoma, while the others had hepatocellular carcinoma, colon adenocarcinoma, and mucinous lung adenocarcinoma. Clinical presentation varied: three patients reported dyspnea, one had chest pain, and one was entirely asymptomatic, with elevated troponin detected during routine monitoring.

Troponin T levels ranged from 292 to 6,019 ng/L (normal ≤15 ng/L), and ECG findings included conduction abnormalities or ventricular ectopy in all cases. Baseline ECGs were not consistently available; when present, comparison suggested that some abnormalities were pre-existing, while others represented new changes during presentation. Echocardiograms revealed preserved ejection fraction in four patients, while one patient had a markedly reduced ejection fraction of 18%.

Cardiac MRI supported the diagnosis of myocarditis in two cases. Endomyocardial biopsy was performed in one patient but did not yield diagnostic findings.

All patients in the series were treated with corticosteroids. Four began therapy with intravenous methylprednisolone at a dose of 1,000 mg per day, while one patient initially received high-dose oral prednisone, which was later switched to an intravenous regimen. Two patients required additional immunosuppressive treatments; one was given intravenous immunoglobulin (IVIG) along with plasmapheresis, and the other received abatacept.

In Case 1, there was concern for myocarditis–myositis–myasthenia gravis overlap. Plasmapheresis was initiated primarily due to concern for progression to myasthenic crisis after the patient developed respiratory failure requiring intubation. The patient underwent four

sessions with subsequent clinical improvement. Creatine kinase was mildly elevated at 505 U/L (reference range 39–308 U/L), supporting concurrent skeletal muscle involvement.

Outcomes differed among the group: three patients recovered, while two unfortunately died. In one case, death occurred months later in the setting of progressive immune-related complications. In the other, respiratory failure and systemic irAEs predominated. While myocarditis may have contributed, definitive attribution was not possible.

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DISCUSSION

ICI myocarditis is diagnostically challenging, as no single test is definitive. Clinical features range from asymptomatic biomarker elevation to fulminant heart failure, malignant arrhythmias, and sudden death [4,5]. Troponin I is preferred over troponin T due to confounding by myositis; higher levels predict major adverse cardiovascular events [9]. In our cohort, only troponin T was routinely available, as troponin I required send-out testing with an approximately one-week turnaround. This may have limited biomarker specificity, particularly in overlap syndromes.

ECG frequently demonstrates new conduction abnormalities in ICI-associated myocarditis. In our series, conduction disturbances or ventricular ectopy were observed in all patients; however, documentation confirming that these changes were newly developed was not consistently available.

TTE may reveal preserved or impaired systolic ejection function. CMR is the most informative noninvasive modality, with the updated 2018 Lake Louise criteria requiring both T2 and T1 based abnormalities supporting robust diagnostic confidence [10].

In Case 3, the presence of severely reduced ejection fraction with apical ballooning raised consideration of Takotsubo syndrome. However, CMR demonstrated mid-myocardial to subepicardial delayed enhancement with associated myocardial edema and mild pericardial enhancement, findings more consistent with nonischemic myopericarditis in the setting of ICI therapy. While Takotsubo cardiomyopathy is a diagnosis of exclusion, overlap cannot be entirely excluded, especially given recovery of ventricular function about two months after the initial admission.

EMB remains the reference standard but is limited by invasiveness and sampling error [10]. The presence of inflammatory cell infiltrates, myocyte necrosis or damage without ischemia, with the use of hematoxylin and eosin (H&E) and immunohistochemistry (IHC) can confirm the diagnosis. Specific criteria include ≥14 leucocytes/mm2 including up to 4 monocytes/mm2 with the presence of CD-3 positive T-lymphocytes ≥7 cells/mm2 [11].

Contemporary cohorts have developed ICI myocarditis risk predictors score for prognosis [11]. These scores are prognostic tools and have not been validated to guide treatment intensity (Table 3). Therefore, they should not be interpreted as directing immunosuppressive escalation or de-escalation strategies.

Patients receiving ICI for active thymoma show markedly higher cardiotoxicity risk, consistent with the autoimmune tendency of thymic tumors and the hypothesis that thymic dysregulation permits autoreactive T cells to target cardio-muscular antigens once checkpoint pathways are blocked [12-15].

Therapeutic principles remain grounded in immediate discontinuation of the checkpoint inhibitor and initiation of corticosteroids as outlined in ASCO guidance (table 2). Lower-grade disease (grades 1–2) is generally treated with oral prednisone 1–2 mg/kg/day, while severe presentations (grade ≥3) warrant intravenous methylprednisolone at 500–1,000 mg/day

for several days followed by a taper. Observational data suggest that early initiation of high-dose steroids is associated with improved outcomes [3,16]. Patients not responding adequately may require second-line therapies such as mycophenolate mofetil, intravenous immunoglobulin, anti-thymocyte globulin, or therapeutic plasma exchange. More recently, selective T-cell co-stimulation blockade with abatacept has emerged as a promising salvage option in fulminant cases [17].

An increasingly recognized entity is the myocarditis myositis myasthenia gravis (MMM) overlap syndrome, a severe presentation that typically occurs early after ICI initiation and carries high mortality. The exact mechanism is unclear; however, it is hypothesized that shared antigenic targets between cardiac, skeletal, and neuromuscular junction tissues contribute to immune-mediated injury [18,19]. Early multidisciplinary management is essential.

This study is limited by its retrospective, single-center design, small sample size, and lack of standardized diagnostic and treatment protocols. Selection bias and variability in follow-up further limit generalizability. Additionally, the observational design precludes causal inference, including definitive attribution of mortality to myocarditis.

CONCLUSION

ICI-associated myocarditis remains an uncommon but potentially serious immune-related adverse event. Diagnosis is often challenging, as confirmation may vary depending on the availability and interpretation of biomarkers, imaging, and histopathology. A structured evaluation that integrates cardiac biomarkers, ECG, TTE, and CMR using the revised Lake Louise criteria can help improve diagnostic confidence, particularly in settings where troponin I is not readily available. In this context, CMR can help distinguish myocardial from skeletal muscle injury, especially when overlap syndromes are suspected [20].

Early discontinuation of the offending agent and prompt initiation of corticosteroids remain the cornerstone of management, in line with current ASCO recommendations [16]. In our cohort, all patients received high-dose corticosteroids regardless of formal ASCO grade. This likely reflects the clinical uncertainty and perceived severity surrounding suspected ICI myocarditis in real-world practice.

Although emerging risk stratification models have identified factors associated with adverse outcomes, these tools were developed for prognostic assessment and should not be viewed as prescriptive treatment algorithms. Recognition of MMM overlap and early multidisciplinary coordination are essential, particularly in more complex presentations. Targeted therapies such as abatacept may have a role in selected refractory cases, but further evidence is needed.

Given the heterogeneity in diagnostic confirmation, cases should be reported with transparent classification (definite, probable, or possible). The present series is descriptive and hypothesis-generating. Larger prospective studies using standardized diagnostic criteria are necessary to better define optimal evaluation and treatment strategies.

Introducere: Inhibitorii punctelor de control imun (ICI) îmbunătățesc prognosticul în diferite tipuri de cancer, însă pot determina reacții adverse imune, inclusiv miocardită asociată tratamentului. Deși rară, aceasta este o complicație potențial severă.

Metode: Am analizat retrospectiv pacienții cu miocardită asociată ICI tratați la Mayo Clinic Florida între anii 2019–2024 și am efectuat o revizuire sistematică a literaturii existente. Cazurile au fost clasificate ca definite, probabile sau posibile miocardită asociată ICI, pe baza criteriilor consensuale (CMR) și a variabilelor histopatologice.

Rezultate: Au fost identificați cinci pacienți cu vârste cuprinse între 74 și 85 de ani, dintre care patru erau bărbați. Miocardita a apărut între 5 și 30 de zile după inițierea terapiei anti-PD-1. Manifestările clinice au inclus dispnee (trei pacienți), durere toracică (un pacient) și supraveghere asimptomatică prin monitorizare de rutină (un pacient). Troponina T a fost crescută peste percentila 99 la toate cazurile (valorile normale <= 15 ng/L). Electrocardiograma (ECG) a evidențiat tulburări de conducere la trei pacienți sau extrasistole ventriculare la un pacient. Fracția de ejecție a ventriculului stâng a fost păstrată la patru pacienți și sever redusă la unul.

Rezonanța magnetică cardiacă (CMR) a furnizat informații de susținere în patru dintre cele cinci cazuri, în timp ce biopsia endomiocardică (EMB) a fost efectuată și nu a demonstrat inflamație activă. Conform criteriilor predefinite, un caz a fost clasificat drept miocardită asociată ICI definită, unul probabilă și trei posibile.

Toți cei cinci pacienți au necesitat tratament cu corticosteroizi. Doi au necesitat imunosupresie suplimentară. Un pacient a dezvoltat concomitent miastenia gravis, compatibilă cu sindromul de suprapunere miocardită–miozită–miastenie (MMM), iar un alt pacient a prezentat pneumonită concomitentă. Trei pacienți s-au recuperat. Doi pacienți au decedat în perioada de urmărire; în ambele cazuri, miocardita a fost considerată un factor contributiv, deşi o relaţie cauzală directă nu a putut fi stabilită cu certitudine.

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IRB was exempted since this was a case series.

References

1. SIEGEL RL, GIAQUINTO AN, JEMAL A. *Cancer statistics, 2024*. CA Cancer J Clin. 2024;74(1):7-33.
2. POSTOW MA, SIDLOW R, HELLMANN MD. *Immune-related adverse events associated with immune checkpoint blockade.* N Engl J Med. 2018;378(2):158-168.
3. SCHNEIDER BJ, NAIDOO J, SANTOMASSO BD, LACCHETTI C, ADKINS S, ANADKAT M, *et al. Management of immune-related adverse events in patients treated with immune checkpoint inhibitor therapy: ASCO guideline update*. J Clin Oncol. 2021;39(36):4073-4126.
4. MAHMOOD SS, FRADLEY MG, COHEN JV, NOHRIA A, REYNOLDS KL, HEINZERLING LM, *et al. Myocarditis in patients treated with immune checkpoint inhibitors.* J Am Coll Cardiol. 2018;71(16):1755-1764.
5. PALASKAS N, LOPEZ-MATTEI J, DURAND JB, ILIESCU C, DESWAL A. *Immune checkpoint inhibitor myocarditis: pathophysiological characteristics, diagnosis, and treatment*. J Am Heart Assoc. 2020;9(2):e013757.
6. LIPE DN, QDAISAT A, KRISHNAMANI PP, PARIKH R, MURTHY P, PATEL M, *et al. Myocarditis, myositis, and myasthenia gravis overlap syndrome associated with immune checkpoint inhibitors: a systematic review*. Diagnostics (Basel). 2024;14(16):1794.
7. BAIK AH, OLUWOLE OO, JOHNSON DB, SHAH N, SALEM JE, TSAI KK, *et al. Mechanisms of cardiovascular toxicities associated with immunotherapies*. Circ Res. 2021;128(11):1780-1801.
8. FERREIRA VM, SCHULZ-MENGER J, HOLMVANG G, KRAMER CM, CARBONE I, SECHTEM U, *et al. Cardiovascular magnetic resonance in*

nonischemic myocardial inflammation: updated Lake Louise criteria. J Am Coll Cardiol. 2018;72(24):3158-3176.

9. ROSSI VA, GAWINECKA J, DIMITRIOU F, *et al. Value of troponin T versus troponin I in the diagnosis of immune checkpoint inhibitor-related myocarditis and myositis.* ESC Heart Fail. 2023;10(4):2680-2685.
10. CAFORIO ALP, PANKUWEIT S, ARBUSTINI E, BASSO C, GIMENO-BLANES J, FELIX SB, *et al. Current state of knowledge on aetiology, diagnosis, management, and therapy of myocarditis.* Eur Heart J. 2013;34(33):2636-2648.
11. DRAZNER MH, BOZKURT B, COOPER LT, AGGARWAL NR, BASSO C, BHAVE NM, *et al. 2024 ACC expert consensus decision pathway on strategies and criteria for the diagnosis and management of myocarditis*. J Am Coll Cardiol. 2024;83:In press.
12. POWER JR, DOLLADILLE C, OZBAY B, PROCUREUR A, EDERHY S, PALASKAS NL, *et al. Immune checkpoint inhibitor-associated myocarditis: a novel risk score.* Eur Heart J. 2025;46:In press.
13. AXELROD ML, MEIJERS WC, SCREEVER EM, QIN J, CARROLL MG, SUN X, *et al. T cells specific for alpha-myosin drive immunotherapy-related myocarditis.* Nature. 2022;611(7936):818-824.
14. CHO J, KIM HS, KU BM, CHOI YL, CRISTESCU R, HAN J, e*t al. Pembrolizumab for patients with refractory or relapsed thymic epithelial tumor: an open-label phase II trial.* J Clin Oncol. 2019;37(24):2162-2170.
15. SHELLY S, AGMON-LEVIN N, ALTMAN A, SHOENFELD Y. *Thymoma and autoimmunity.* Autoimmun Rev. 2011;10(12):753-758.
16. PALASKAS NL, SIDDIQUI BA, DESWAL A. *Steroids in immune checkpoint inhibitor myocarditis*. JACC CardioOncol. 2024;6(5):800-803.

17. SALEM JE, ALLENBACH Y, VOZY A, BRECHOT N, JOHNSON DB, MOSLEHI JJ, *et al. Abatacept for severe immune checkpoint inhibitor–associated myocarditis*. N Engl J Med. 2019;380(24):2377-2379.
18. SÁNCHEZ-CAMACHO A, FERREIRA VM, LYON AR, *et al. Management of immune-related myocarditis, myositis and myasthenia gravis overlap syndrome*. Front Immunol. 2025;16:1597259.
19. SUZUKI S, UTSUGISAWA K, YOSHIKAWA H, NAGANE Y, SATOH T, KUWANA M, *et al. Autoimmune targets of heart and skeletal muscles in myasthenia gravis.* Arch Neurol. 2009;66(11):1334-1338.
20. GANATRA S, BARAC A, ARMENIAN S, *et al. Diagnosis and management of cardiovascular adverse effects of targeted oncology therapies: Bruton's tyrosine kinase, immune checkpoint, and vascular endothelial growth factor inhibitors: 2025 ACC concise clinical guidance.* J Am Coll Cardiol. 2026;87(5):654–682.

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TABLES:

Case	Age/Sex	Malignancy	ICI & Timing	Presentation	Peak troponin normal ≤15 ng/L	±ECG	Echo (LVEF)	CMR/Biopsy	Therapy	Classification *	Outcome
1	74/M	RCC	Nivolumab + cabozantinib; approx 30 d	Dyspnea; MMM overlap (myasthenia)	1,871	Sinus brady; NSVT	Preserved; LVH	CMR deferred	High dose steroids; IVIG; plasmapheresis (for myasthenia)	Possible myocarditis	Recovery
2	82/M	Urothelial/RCC	Nivolumab; 28 d	Dyspnea	1,155	RBBB; LAFB; 1° AV block	Preserved	Biopsy: hypertrophic changes; no active inflammation	High dose steroids; abatacept (stopped)	Possible myocarditis	Recovery
3	62/M	Hepatocellular carcinoma	Nivolumab; 23 d	Chest pain; ST elevation	408	RBBB; QT prolongation	EF 18%; apical ballooning	CMR: non-ischemic myopericarditis	High dose steroids	Probable myocarditis	Death (6 months)
4	82/F	Colon adenocarcinoma	Pembrolizumab; recent	Respiratory failure; VT	6,019	Wide QRS; LBBB; PVCs	EF 64%	CMR not done; angiography declined	High dose steroids	Possible myocarditis	Death (comfort care)
5	73/M	Lung mucinous adenocarcinoma	Pembrolizumab; after 3 cycles	Asymptomatic biomarker rise	292	PACs; RBBB	Normal	CMR: focal LGE & edema	High-dose steroids (escalated from oral to IV)	Definitive myocarditis	Recovery

Table 1. Summary of Clinical Cases

***Classification:** Definite = CMR meeting revised 2018 Lake Louise criteria or diagnostic EMB; Probable = elevated troponin with supportive but non-diagnostic imaging; Possible = elevated troponin with compatible clinical features but no confirmatory imaging or biopsy.

±Baseline ECG comparison: Case 1 and Case 5 had no prior ECG available. Case 2 had ECG findings similar to baseline. Case 3 had baseline right bundle branch block and right axis deviation with new precordial ST elevations. Case 4 had baseline LBBB with premature ventricular complexes, with new wide-complex tachycardia (approximative 140 bpm) on presentation.

Grade	Clinical description (concise)	Recommended management (ASCO)
1	Asymptomatic biomarker elevation; normal ECG/Echo	Hold ICI; oral prednisone 1-2 mg/kg/day; close monitoring; escalate if no response [2].
2	Mild symptoms or new ECG/Imaging changes	Hold ICI; oral prednisone 1-2 mg/kg/day; cardiology involvement; consider admission; gradual taper [2].
3	Severe symptoms, arrhythmias, or LV dysfunction	Permanently discontinue ICI; pulse IV methylprednisolone 500-1,000 mg/day for 3–5 days; transition to taper; add second-line immunosuppression if refractory [2].
4	Life-threatening; hemodynamic compromise	ICU care; pulse IV steroids; early second-line therapy (mycophenolate, IVIG, ATG, plasmapheresis); consider abatacept as rescue in refractory cases [2,9,10].

Table 2. ASCO Cardiovascular irAE (Myocarditis) Grading and Management.

Parameter	Points
Underlying thymoma	2
Coexisting skeletal muscle or neuromuscular involvement	1
Low QRS voltage on ECG (≤0.5 mV, Sokolow–Lyon)	1
Depressed left ventricular systolic function (LVEF <50%)	1
Mild–moderate troponin elevation (approximative 20–200 × ULN)	1
Marked troponin elevation (approximative \200–2000 × ULN)	2
Extreme troponin elevation (>2000 × ULN)	3

Table 3. Proposed Clinical Risk Score for ICI-Myocarditis (adapted from Power JR et al., Eur Heart J 2025) ULN = upper limit of normal. Score values correspond to weighted risk of major adverse cardiac events.

Score = 0: ICI interruption alone; immunosuppression generally not required; no major events observed at 1 month.

Score = 1: Consider inpatient monitoring.

Score ≥2: High risk early immunosuppression strongly advised.

* Risk scores are prognostic and have not been validated to guide immunosuppressive escalation or de-escalation. While higher scores are associated with increased rates of adverse outcomes, they should not be used to direct treatment intensity.

Appendix – Detailed Case Summaries

Case 1.

A 74-year-old man with metastatic renal cell carcinoma on nivolumab + cabozantinib developed dyspnea and ptosis approximative 30 days after initiation. Troponin peaked at 1,871 ng/L. ECG showed sinus bradycardia and non-sustained supraventricular tachycardia; echocardiogram revealed concentric hypertrophy with preserved EF. CMR was deferred. He was treated with IV methylprednisolone (1 g × 3 days), IVIG, and pyridostigmine. Due to concomitant myasthenia gravis/myocarditis overlap, plasmapheresis was performed. He improved and was discharged with recovery.

Case 2.

An 82-year-old man with urothelial carcinoma (status post-nephrectomy) developed dyspnea 28 days after nivolumab. Troponin peaked at 1,155 ng/L. ECG showed RBBB, LAFB, and first-degree AV block; echocardiogram showed preserved EF. CMR revealed subtle T2 signal; biopsy demonstrated hypertrophic changes without inflammation. He was treated with high-dose IV steroids and later abatacept (discontinued for lack of efficacy). His respiratory course was prolonged, requiring tracheostomy, but he recovered without myocarditis recurrence.

Case 3.

A 62-year-old man with hepatocellular carcinoma presented 23 days after nivolumab with chest pain, nausea, and ST-elevation. Troponin rose to 408 ng/L. ECG showed RBBB, QT prolongation, and right axis deviation. Echocardiogram demonstrated EF 18% with apical ballooning. Angiography was normal. CMR confirmed non-ischemic myopericarditis. He

received high-dose steroids but later developed recurrent pneumonitis; transitioned to palliative care. He died six months later.

Case 4.

An 82-year-old woman with colon adenocarcinoma developed acute respiratory failure and ventricular tachycardia after two cycles of pembrolizumab. Troponin peaked at 6,019 ng/L. ECG showed LBBB with PVCs; echocardiogram revealed preserved EF (64%). CTA was negative; CMR could not be performed; angiography was declined. She was empirically treated with high-dose steroids, but progressed to renal and respiratory failure. Comfort measures were instituted, and she died.

Case 5.

A 73-year-old man with mucinous lung adenocarcinoma presented with isolated troponin elevation (292 ng/L) after three cycles of pembrolizumab. ECG showed RBBB and PACs; echocardiogram was normal. CMR demonstrated patchy late gadolinium enhancement and edema. He was initially treated with oral prednisone but escalated to IV methylprednisolone due to rising troponins. Symptoms resolved, and he was discharged without recurrence.

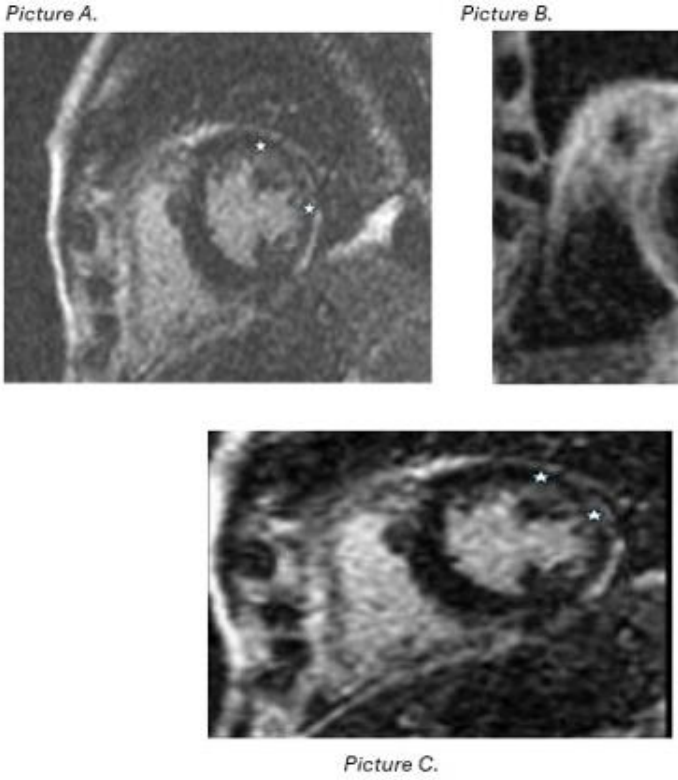

Figure 1: Cardiac magnetic resonance (CMR) with gadolinium showing Myocarditis from patient in case #4. Picture A. CMR with gadolinium contrast reveals no evidence of first-pass perfusion abnormalities. Picture B. Mid-myocardial to subepicardial linear late gadolinium enhancement (LEG) is present in the lateral and inferior walls at the mid-apical level. Picture C. There is associated lateral wall myocardial edema. Findings are most consistent with a nonischemic myocarditis

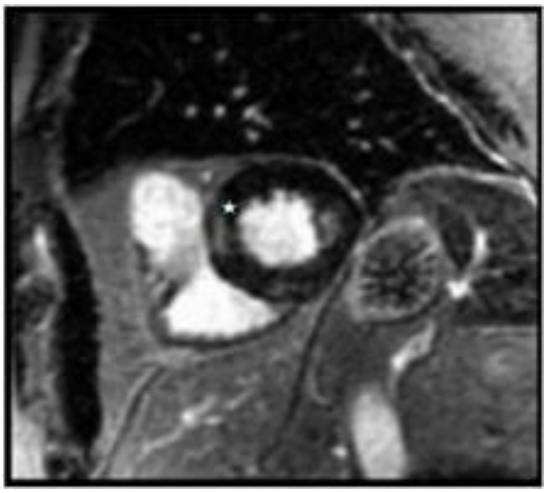

Figure 2: Myocardial imaging (MR) from patient in case #5 showing patchy focal late gadolinium enhancement.(LGE) with subtle edema in the basal and mid-inferior segments of the left ventricle as depicted by the star in the image.