ESC European Society of Cardiology

European Heart Journal - Case Reports (2025) **9**, ytae665
https://doi.org/10.1093/ehjcr/ytae665

CASE REPORT
Heart failure

Fulminant immune checkpoint inhibitor-associated myocarditis bridged to recovery with a temporary left ventricular assist device: a case report

Quinn Mallery *, Kevin Walsh, Mark Pelka, Ivo Genev, and Amir Darki

Cardiology Department, Loyola University Medical Center, 2160 S 1st Ave, Maywood, IL 60153-3328, USA

Received 20 May 2024; revised 20 July 2024; accepted 12 November 2024; online publish-ahead-of-print 13 December 2024

Background Immune checkpoint inhibitors (ICIs) are effective antineoplastic agents but can cause adverse effects in many organ systems. Cardiovascular toxicities include arrhythmias, myocarditis, heart failure, takotsubo syndrome, pericarditis, coronary artery disease, and vasculitis.

Case summary A 66-year-old woman with Stage 3C2 endometrial carcinoma presented for her second cycle of pembrolizumab, carboplatin, and paclitaxel. She subsequently suffered cardiac arrest and was brought to the emergency department. Spontaneous circulation returned following resuscitation, but she was haemodynamically unstable. An electrocardiogram revealed complete heart block. Initial management included intubation, vasopressor support, and transcutaneous pacing before transfer to the catheterization lab. Coronary angiography revealed no coronary artery disease. Right heart catheterization confirmed severe cardiogenic shock despite inotropic support and a temporary transvenous pacemaker in place. A micro-axial flow pump (Impella CP) was implanted for deteriorating cardiogenic shock. She was treated with high-dose corticosteroids (dexamethasone 190 mg i.v.) for suspected ICI-associated myocarditis, with significant improvement in cardiac function. The Impella was weaned and removed on Day 5. Cardiac magnetic resonance imaging showed elevated T1 and T2 signal intensities, consistent with the 2018 Lake Louise Criteria for myocarditis. The complete heart block was resolved, but a leadless pacemaker was implanted due to pre-existing conduction abnormalities.

Discussion Early recognition of ICI-associated myocarditis can be achieved with biochemical testing, electrocardiography, imaging, and expedited investigation of alternative causes for cardiac decompensation. Our case demonstrates that temporary left ventricular assist devices can support cardiac output for patients in cardiogenic shock due to ICI-associated myocarditis, allowing for recovery following high-dose corticosteroids.

Keywords Cardiogenic shock • Myocarditis • Immune checkpoint inhibitors • Immune checkpoint inhibitors • Left ventricle assist device

ESC curriculum 2.3 Cardiac magnetic resonance • 3.4 Coronary angiography • 6.4 Acute heart failure

* Corresponding author. Tel: +952 454 2540, Fax: +708 216 6890, Email: qmallery@gmail.com
Handling Editor: Josip Andelo Borovac
Peer-reviewers: Niklas Schenker; Aiste Monika Jakstaite
Compliance Editor: Ralph Mark Louis Neijenhuis

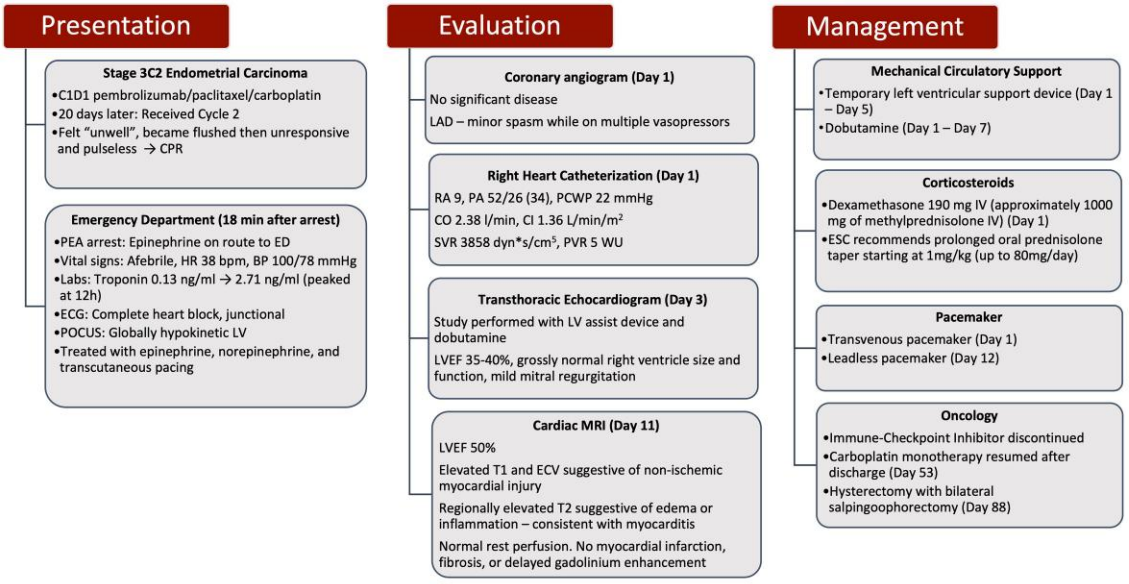
Learning points

- Immune checkpoint inhibitors (ICIs) are increasingly common antineoplastic agents with the potential to cause cardiotoxicity. This can present as arrhythmia, pericarditis, and myocarditis with symptoms ranging from mild to fulminant cardiogenic shock.
- Management of ICI-associated myocarditis includes early recognition, ICI treatment cessation, and high-dose corticosteroids followed by a prolonged prednisone taper. Patients with fulminant myocarditis can be effectively supported through recovery with temporary left ventricular assist devices.

Introduction

Immune checkpoint inhibitors (ICIs) are an exciting development in cancer treatment that allows for native T-cell-mediated destruction of cancer cells. Although rare, ICI-associated cardiotoxicity has been reported in case series. Death from cardiovascular causes in this population is common, ranging from 17 to 27%.[1,2] Extracorporeal membrane oxygenation has been previously reported as a viable means to provide haemodynamic support during immunosuppressant treatment, although alternative means of cardiac support, such as temporary left ventricular assist devices, are less well described.[3]

Summary figure



Cardiopulmonary resuscitation CPR, Pulseless electrical activity PEA, Emergency Department ED, Electrocardiogram ECG, Point of Care Ultrasound POCUS, Left Anterior Descending LAD, right atrium RA, pulmonary artery PA, pulmonary capillary wedge pressure PCWP, cardiac output CO, cardiac index CI, systemic vascular resistance SVR, pulmonary vascular resistance PVR, left ventricle LV, ejection fraction EF, extracellular volume ECV

Case presentation

A 66-year-old woman with Stage 3C2 endometrial carcinoma presented to an outpatient chemotherapy center for her second cycle of pembrolizumab, carboplatin, and paclitaxel. Medical history included breast cancer in remission for 20 years and anthracycline-induced cardiac dysfunction with a mild global reduction of left ventricular (LV) ejection fraction (LVEF) of 45%. Her oncologist was aware of the cardiomyopathy, and due to the low incidence of cardiotoxicity, believed she would likely benefit from immunotherapy. After completion of the pembrolizumab infusion, she collapsed to the ground and was found to be in cardiac arrest. Paramedics determined she was in pulseless electrical activity arrest and treated her accordingly during transport. On examination in the emergency department, she remained unconscious but had a palpable pulse, heart rate of 38 b.p.m., and a blood pressure of 100/78 mmHg on epinephrine and norepinephrine support. She was intubated for airway protection, and the initial arterial blood gas showed a pH 7.24 (normal range 7.36–7.46), pCO2 30 mmHg (normal range 32–46 mmHg), and pO2 271 mmHg (normal range 83–108 mmHg). Lactate was 9.2 mmol/L (normal range 0.4–1.3 mmol/L). Troponin I was 0.13 ng/mL (normal < 0.03 ng/mL). The initial electrocardiogram (ECG) showed complete heart block (*Figure 1*), and transcutaneous pacing was initiated prior to transfer to the cardiac catheterization lab.

Coronary angiography demonstrated a minor spasm in the left anterior descending artery in the setting of multiple pressors but no significant coronary artery disease (*Figure 2*). Right heart catheterization on vasopressor support demonstrated a mean right atrial pressure of 9 mmHg (normal range 1–5 mmHg), pulmonary artery pressure 52/26 (34) mmHg (normal range systolic 15–30, diastolic 4–12, and mean 9–19 mmHg), pulmonary capillary wedge pressure 22 mmHg (normal range 4–12 mmHg), cardiac index 1.36 L/min/m^2 (normal range 2.5–4.0 L/min/m^2), and cardiac output 2.38 L/min (normal range

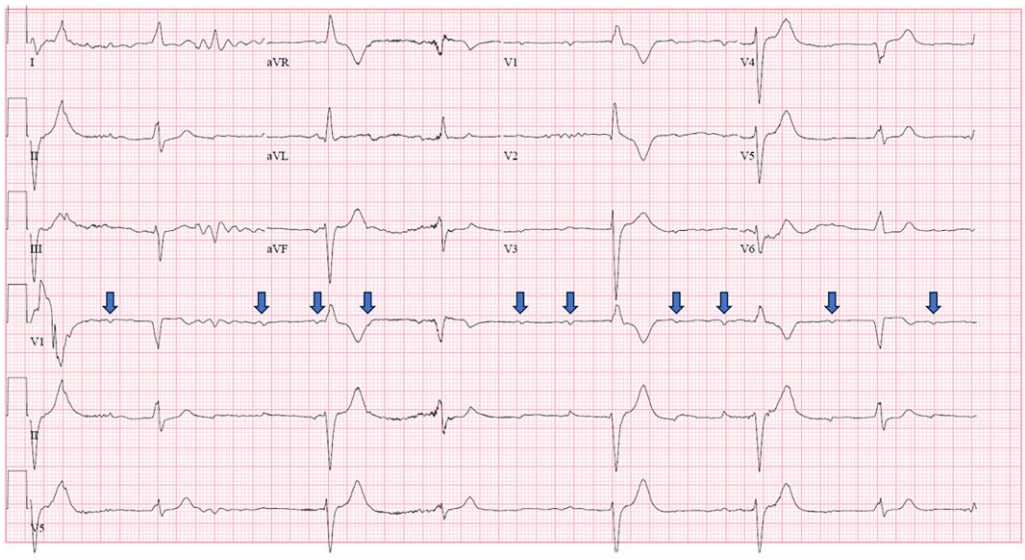


Figure 1 Complete heart block on presentation. Electrocardiogram demonstrating atrioventricular dissociation, junctional beats, and premature ventricular contractions are present.

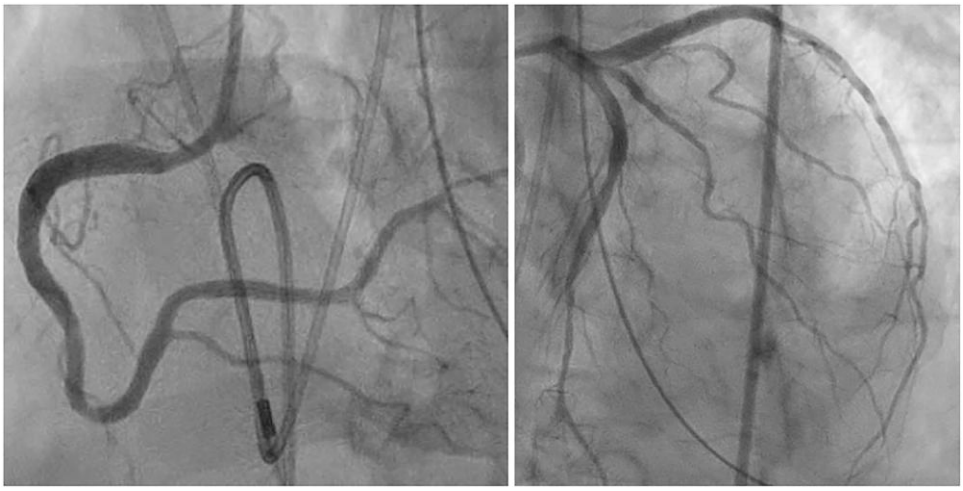


Figure 2 Coronary angiography. Left panel showing the right coronary artery in the left anterior oblique view. Right panel showing the left anterior descending and left circumflex arteries from the right anterior oblique view. There is no significant stenosis visualized.

4–8 L/min). A temporary transvenous pacemaker (TVP) was placed without significant improvement in vasopressor requirements or haemodynamics. Given clinical findings consistent with the Society of Cardiovascular Angiography and Interventions Stage D cardiogenic shock, the decision was made to place a micro-axial flow pump (Impella CP, Abiomed, MA, USA). Following the successful placement, cardiac output (index) improved to 6.8 L/min (3.9 L/min/m^2).

Upon admission to the cardiac care unit, the advanced heart failure team was consulted. Due to suspicion of ICI-associated myocarditis, she received high-dose corticosteroid therapy with dexamethasone 190 mg i.v. (~1000 mg methylprednisolone). Given the strong clinical evidence supporting ICI-associated myocarditis, endomyocardial biopsy was deemed unlikely to change clinical management and was deferred. A transthoracic echocardiogram (TTE) showed a reduced LVEF between 35 and 40%, grossly normal right ventricle size and function, and no pericardial effusion (Supplementary material online, *Video S1*). Dobutamine 5 mc/kg/min was added for inotropic support. By Day 2, the patient's lactate normalized and the cardiac index calculated using the Fick equation was 4.4 L/min/m^2 on power level 7. The complete heart block resolved to sinus tachycardia. The Impella power was weaned slowly while monitoring mixed venous oxygen saturations until Day 4 when the patient was tolerating power level 3. The Impella and TVP were removed on Day 5. Her mental status improved, and she was extubated on Day 6.

She was subsequently transferred to the cardiology floor where guideline-directed medical therapy was resumed or initiated including metoprolol–succinate 25 mg, sacubitril/valsartan 97–103 mg, spironolactone 25 mg, and dapagliflozin 10 mg. On Day 11, cardiac magnetic resonance (CMR) imaging demonstrated globally elevated T1 signal intensity and increased extracellular volume in the LV, suggestive of non-ischaemic myocardial injury (*Figure 3*). Additionally, there was regionally elevated T2 signal intensity, indicative of myocardial oedema (*Figure 4*). The LVEF had improved to 50%, and there was no delayed gadolinium enhancement, further ruling out ventricular scarring or prior infarct. These CMR findings met the 2018 Lake Louise Criteria for myocardial inflammation.[4]

There was concern that a baseline left bundle branch block contributed to the complete heart block. Therefore, after shared decision-making, she underwent leadless pacemaker implantation prior to discharge. A leadless pacemaker was chosen in part due to reduced infection risk while undergoing chemotherapy. Our patient had a favourable neurologic outcome with no residual neurologic deficits. Although recommended in the European Society of Cardiology guidelines, there was no prolonged steroid taper prescribed on discharge.

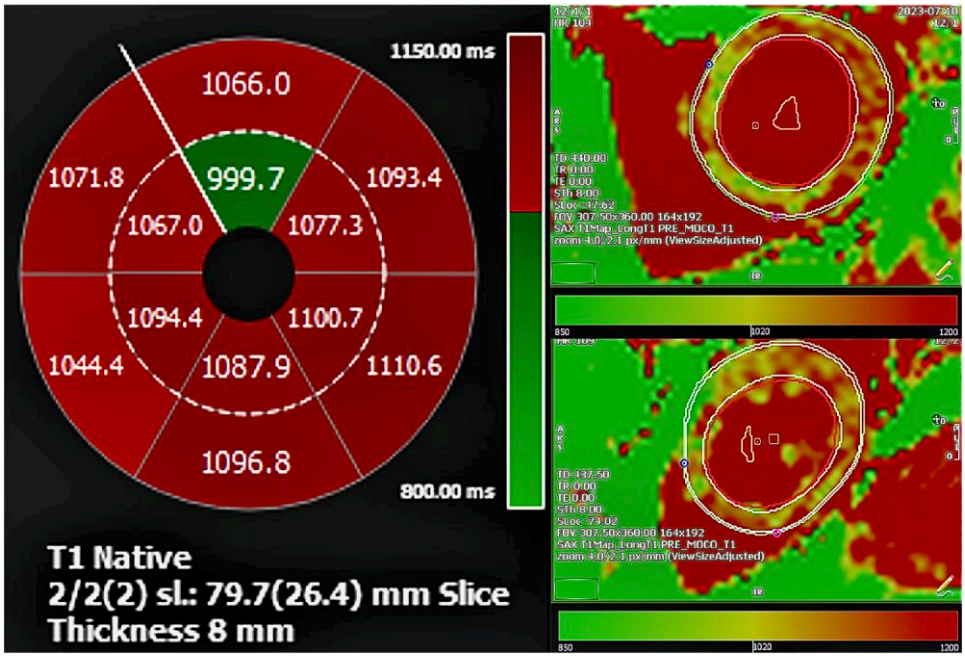


Figure 3 Cardiac magnetic resonance imaging T1 mapping. T1-weighted short-axis view demonstrating globally elevated T1 signal intensity, suggestive of non-ischaemic myocardial injury (diffuse fibrosis/infiltration).

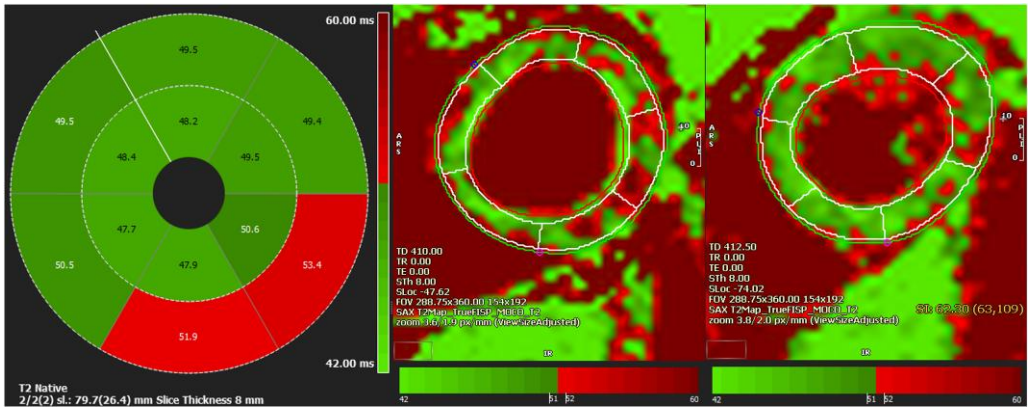


Figure 4 Cardiac magnetic resonance imaging T2 mapping. T2-weighted short-axis view demonstrating elevated T2 signal intensity in the basal inferolateral region, indicative of oedema.

At 1-month follow-up, her B-natriuretic peptide was 40 pg/mL (normal range 1–100 pg/mL), pacemaker interrogation showed 0% ventricular pacing, and TTE showed an LVEF of 40%. She resumed endometrial carcinoma treatment with carboplatin monotherapy prior to successful total hysterectomy with bilateral salpingo-oophorectomy. At her most recent follow-up, 1-year post-discharge, her oncologist reported no evidence of disease, and she remained active with New York Heart Association Class II heart failure symptoms.

Discussion

Immune checkpoint inhibitor-associated cardiotoxicity is rare; however, immunotherapy is becoming a more common modality for the treatment of a variety of malignant cancers.[5] The most common presentation of cardiotoxicity includes congestive heart failure; however, ~23% of patients may present with cardiac conduction abnormalities alone.[1] In prior case series, patients treated with corticosteroids had a higher rate of LV function recovery and lower doses of steroids were associated with higher major adverse cardiac events (MACE) rates.[1,2]

Diagnosis of myocarditis in the setting of ICIs requires ruling out a variety of alternative diagnoses. Bonaca *et al.*[6] have proposed separate categories for definite, probable, and possible myocarditis. To diagnose definite myocarditis without tissue pathology, the patient must have a clinical syndrome consistent with myocarditis and either a diagnostic CMR or new wall motion abnormalities on echocardiogram not explained by an alternative cause. When using echocardiography to diagnose, the patient must also have elevated biomarkers of cardiac myonecrosis, ECG evidence of myo-pericarditis, and negative angiography excluding obstructive coronary disease. Patients with a diagnostic CMR are only required to have elevated cardiac biomarkers or ECG evidence.

The European Society of Cardiology has published clinical practice guidelines for the evaluation and management of ICI-associated myocarditis.[7] Workup should include troponin levels, ECG, and cardiovascular imaging (echocardiography and CMR). Endomyocardial biopsy should be considered if the diagnosis is suspected but not confirmed with imaging and biomarkers. Acute management includes discontinuing the ICI, high-dose corticosteroids initiated rapidly (500–1000 mg of methylprednisolone i.v. for 3–5 days), and consideration of immunosuppressant escalation (mycophenolate mofetil, anti-thymocyte globulin, intravenous immunoglobulin, etc.) if there is no response. If there is clinical improvement, patients should transition to oral prednisolone starting at 1 mg/kg up to 80 mg/day for a prolonged taper with interval monitoring of TTE and cardiac biomarkers.

Recognition of ICI-associated myocarditis and expedited investigation of alternative causes for cardiac decompensation are essential for achieving favourable outcomes. Our case shows that temporary LV assist devices can effectively support cardiac output in cardiogenic shock while allowing time for recovery following high-dose corticosteroids.

Lead author biography

Quinn Mallery, MD, MPH, is an internal medicine resident at Loyola University Medical Center. He earned his Bachelor of Science from the University of Wisconsin-Madison, his Master of Public Health from the University of Minnesota-Twin Cities, and his medical degree from the Medical College of Wisconsin. He will be pursuing a fellowship in cardiovascular disease at Loyola University post-residency.

Supplementary material

Supplementary material is available at *European Heart Journal – Case Reports* online.

Consent: Informed consent was obtained according to institutional requirements and COPE guidelines.

Conflict of interest: None declared.

Funding: None declared.

Data availability

All available data have been presented within the manuscript.

References

1. Escudier M, Cautela J, Malissen N, Ancedy Y, Orabona M, Pinto J, et al. Clinical features, management, and outcomes of immune checkpoint inhibitor-related cardiotoxicity. *Circulation* 2017;**136**:2085–2087.
2. 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**:1755–1764.
3. Stein-Merlob AF, Hsu JJ, Colton B, Berg CJ, Ferreira A, Price MM, et al. Keeping immune checkpoint inhibitor myocarditis in check: advanced circulatory mechanical support as a bridge to recovery. *ESC Hear Fail* 2021;**8**:4301–4306.
4. Ferreira VM, Schulz-Menger J, Holmvang G, Kramer CM, Carbone I, Sechtem U, et al. Cardiovascular magnetic resonance in nonischemic myocardial inflammation: expert recommendations. *J Am Coll Cardiol* 2018;**72**:3158–3176.
5. Lee JB, Kim HR, Ha SJ. Immune checkpoint inhibitors in 10 years: contribution of basic research and clinical application in cancer immunotherapy. *Immune Netw* 2022;**22**:e2.
6. Bonaca MP, Olenchock BA, Salem JE, Wiviott SD, Ederhy S, Cohen A, et al. Myocarditis in the setting of cancer therapeutics: proposed case definitions for emerging clinical syndromes in cardio-oncology. *Circulation* 2019;**140**:80–91.
7. Pudil R, Danzig V, Veselý J, Málek F, Táborský M, Elbl L, et al. 2022 ESC guidelines on cardio-oncology developed in collaboration with the European Hematology Association (EHA), the European Society for Therapeutic Radiology and Oncology (ESTRO) and the International Cardio-Oncology Society (IC-OS). *Cor Vasa* 2023;**65**:350–434.