ISSN: 2584-0355
DOI: doi.org/10.51219/MCCRJ/Paola-Montalvão-Corrêa/279

URF PUBLISHERS
connect with research world

Medical & Clinical Case Reports Journal

https://urfpublishers.com/journal/case-reports

Vol: 3 & Iss: 3

Review

Cardiac Toxicities Induced by Immunotherapy: A Brief Review

Paola Montalvão Corrêa*, Edmilson Cunha de Camargo Junior, Maísa Lopes de Menezes, Isabella Valéria Frizon, Maria Clara Bellusci Victorino, Maria Cecília Klosienski, Samia Nicolau Brugnolo, Amanda Marutti Feltrin, Isabela Matos de Oliveira, Gabriela Nunnenmacher, Maria Eduarda Binde, Daphine Ramella Marcon and Ian Caldeira Ruppen

Centro Universitário Ingá - Uningá, Maringá, PR, Brazil

Citation: Corrêa PM, Junior ECC, de Menezes ML, et al. Cardiac Toxicities Induced by Immunotherapy: A Brief Review. *Medi Clin Case Rep J* 2025;3(3):1065-1066. DOI: doi.org/10.51219/MCCRJ/Paola-Montalvão-Corrêa/279

Received: 09 July, 2025; **Accepted:** 11 July, 2025; **Published:** 14 July, 2025

***Corresponding author:** Paola Montalvão Corrêa, Centro Universitário Ingá - Uningá, Maringá, PR, Brazil

ABSTRACT

Immunotherapies, particularly immune checkpoint inhibitors (ICIs), have revolutionized the treatment of various malignant tumors by reactivating antitumor immune responses. However, excessive activation of the immune system can trigger immune-mediated adverse events, among which cardiac toxicities are included. Although rare, these complications which encompass myocarditis, pericarditis, arrhythmias, and heart failure carry high morbidity and mortality when not diagnosed and managed promptly. Immune-mediated myocarditis, though reported in less than 1% of patients treated with ICIs, has a mortality rate exceeding 50% in severe cases, underscoring the need for continuous monitoring and multidisciplinary management protocols. Various biomolecular and imaging markers have been evaluated for early diagnosis, including B-type natriuretic peptide (BNP), cardiac troponins, and cardiac magnetic resonance imaging with late gadolinium enhancement. Management is based on temporary or permanent discontinuation of immunotherapy combined with high-dose corticosteroids; additional therapies such as azathioprine and intravenous immunoglobulin may be instituted in refractory cases. Protocols for reintroducing ICIs after severe cardiac toxicity remain controversial and require case-by-case assessment. This review critically examines current evidence on the epidemiology, pathophysiology, diagnosis, and management of immunotherapy-related cardiac toxicities, proposing guidelines for early identification and therapeutic strategies aimed at reducing morbidity and mortality associated with these adverse events.

Keywords: Immunotherapy; Cardiotoxicity; Myocarditis; Checkpoint inhibitors; Cardiac safety

Introduction

The advent of immune checkpoint inhibitors (ICIs) has markedly improved outcomes for patients with advanced malignancies, including melanoma, lung cancer, and renal cell carcinoma[1,2]. Agents targeting CTLA-4 (ipilimumab) and PD-1/PD-L1 (pembrolizumab, nivolumab, atezolizumab) reinvigorate anergic T lymphocytes, thereby eliciting robust antitumor responses. Despite these significant clinical benefits, disrupting immune tolerance can lead to immune-mediated toxicities across multiple organ systems, known as immune-related adverse events (irAEs). While dermatologic, gastrointestinal, endocrine, and hepatic irAEs are most common, cardiac toxicities, though less frequent, can be rapidly fatal[3]. Population-based studies estimate ICI-associated myocarditis incidence at under 1%, yet symptomatic cases may exceed a

50% mortality rate without immediate intervention[4,5]. Beyond myocarditis, reported manifestations include pericarditis, brady- and tachyarrhythmias, conduction blocks, and heart failure. The underlying pathophysiology involves lymphocytic infiltration of the myocardium, release of proinflammatory cytokines, and direct myocyte injury[6]. Preclinical murine models lacking PD-1 regulation have demonstrated fulminant myocarditis, confirming the critical role of checkpoint pathways in cardiac immune homeostasis[7,8].

Objectives

This work aims to review the recent literature on immunotherapy-induced cardiac toxicities, with emphasis on epidemiology, pathophysiological mechanisms, diagnostic criteria, and management strategies.

Materials and Methods

A systematic literature review was conducted in PubMed, Embase, and the Cochrane Library, covering publications from January 2015 through December 2024.

Discussion

Immune-mediated cardiac toxicities represent a serious yet underrecognized complication of ICI therapy. Underreporting is attributed to nonspecific clinical presentations and the lack of standardized screening protocols[9]. Recent studies indicate that the combined elevation of troponin and B-type natriuretic peptide enhances the predictive value for myocarditis. Cardiac magnetic resonance imaging with late gadolinium enhancement demonstrates over 80% sensitivity and more than 90% specificity for ICI-associated myocarditis. Management centered on intensive immunosuppression has significantly reduced mortality but may attenuate antitumor efficacy. Optimal corticosteroid dosing and tapering schedules remain subjects of debate; current protocols recommend a slow taper over four to six weeks to prevent relapse[10]. In refractory cases, second-line immunosuppressants such as azathioprine and mycophenolate mofetil have shown partial response rates around 60%.

Re-challenge with ICIs following severe cardiac toxicity poses a clinical dilemma[11]. Case reports suggest that select patients achieving full recovery may tolerate subsequent ICI cycles under rigorous monitoring, yet robust controlled data are lacking[12,13]. Switching ICI classes (e.g., from anti-CTLA-4 to anti-PD-1) remains experimental and should be confined to specialized centers. Emerging strategies involve pre-treatment immunoprofiling to identify high-risk individuals such as those with anti-cardiac autoantibodies or elevated memory CD8+ T-cell counts[14]. Future clinical trials should focus on prognostic biomarkers and preventive interventions, potentially leveraging targeted immunosuppressants (e.g., anti-IL-6 or anti-CD20 antibodies). The development of consensus guidelines across oncology and cardiology societies, alongside the establishment of dedicated cardio-oncology units, is essential to optimize patient care and disseminate best practices[15].

Conclusion

Although uncommon, immunotherapy-related cardiac toxicities carry high mortality and necessitate active surveillance, early diagnosis, and multidisciplinary management. Immune-mediated myocarditis is the most lethal manifestation, warranting screening protocols based on troponin and natriuretic peptide monitoring, complemented by targeted imaging studies. Initial treatment with high-dose corticosteroids is critical, with additional immunosuppressive agents reserved for refractory cases. Decisions regarding ICI reintroduction must balance individual risk–benefit considerations, ideally within specialized cardio-oncology centers. Future research should explore risk biomarkers and preventive measures to mitigate the incidence and severity of cardiac irAEs, ensuring patient safety without compromising antitumor efficacy. Collaborative efforts between oncologists and cardiologists, underpinned by clear guidelines, will be pivotal in advancing the management of patients undergoing immunotherapy.

References

1. Bonaca MP, et al. Myocarditis in patients treated with immune checkpoint inhibitors. J American College of Cardiology 2019;73(18):2081-2090.
2. Brahmer JR, et al. Management of immune-related adverse events in patients treated with immune checkpoint inhibitor therapy: ASCO guideline update. J Clin Oncology 2018;36(17):1714-1768.
3. Ganatra S, Neilan TG. Immune checkpoint inhibitor-associated myocarditis. Oncologist 2018;23(8):879-886.
4. Gupta A, et al. Azathioprine for management of immune checkpoint inhibitor-induced myocarditis: a case series. European Heart J - Case Rep 2020;4(3):1-5.
5. Hundal P, et al. Role of cardiac magnetic resonance imaging in diagnosis of immune checkpoint inhibitor myocarditis. JACC: Cardiovascular Imaging 2019;12(12):2482-2484.
6. Johnson DB, et al. Cardiotoxicity associated with immune checkpoint inhibition and exercise: a case series. J Immuno-Therapy of Cancer 2016;4(1):84.
7. Larkin J, Sileni VC, Gonzalez R, et al. Combined nivolumab and ipilimumab or monotherapy in untreated melanoma. New Eng J Med 2015;373(1):23-34.
8. Lyon AR, Yousaf N, Battisti NML, et al. Immune checkpoint inhibitor-related cardiotoxicity: a systematic review. European Heart J 2018;39(36):3121-3131.
9. Mahmood SS, Fradley MG, Cohen JV, et al. Myocarditis in patients treated with immune checkpoint inhibitors. J American College of Cardiology 2018;71(16):1755-1764.
10. Pathiraja P, et al. Role of PD-1 in regulation of autoimmune myocarditis. J Autoimmunity 2019;101:11-18.
11. Postow MA, Sidney L, Schoenfeld JD. Immune-related adverse events associated with immune checkpoint blockade. New Eng J Med 2018;378(2):158-168.
12. Ribas A, Wolchok JD. Cancer immunotherapy using checkpoint blockade. Sci 2018;359(6382):1350-1355.
13. Salem JE, Manouchehri A, Moey M, et al. Cardiovascular toxicities associated with immune checkpoint inhibitors: an observational, pharmacovigilance study. The Lancet Oncology 2018;19(12):1579-1589.
14. Topalian SL, Hodi FS, Brahmer JR, et al. Safety, activity, and immune correlates of anti-PD-1 antibody in cancer. New Eng J Med 2015;366(26):2443-2454.
15. Wang DY, Salem J, Cohen JV, et al. Fatal toxic effects associated with immune checkpoint inhibitors: a systematic review and meta-analysis. JAMA Oncology 2020;6(12):1579-1587.