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Is Every Troponin Rise Myocarditis? Diagnostic Challenges During Immune Checkpoint Inhibitor Therapy

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KEYWORDS: immune checkpoint inhibitor therapy, myocarditis, troponin, pembrolizumab.

CITATION: Cardiol Croat. 2026;21(11-12):363. | https://doi.org/10.15836/ccar2026.363

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Introduction: Immune checkpoint inhibitor (ICI)-associated myocarditis is a rare but potentially life-threatening complication of cancer therapy, typically occurring early during the treatment. Its diagnosis remains challenging owing to the non-specific clinical presentation and the overlap of findings with other causes of myocardial injury.[1-3] We report two cases of suspected ICI myocarditis in patients treated with pembrolizumab.

Case report: *Case 1.* 68-year-old woman receiving maintenance pembrolizumab and bevacizumab for advanced cervical cancer presented to another hospital with fever, chills and upper respiratory tract symptoms two weeks after her last pembrolizumab dose. Left-sided pneumonia was diagnosed, accompanied by a marked rise in high-sensitivity cardiac troponin I (hs-cTnI; peak 651 ng/L). Echocardiography showed preserved left ventricular ejection fraction (LVEF) and a minimal pericardial effusion. After antibiotic therapy, she was referred to our department for further work-up. Coronary angiography revealed an intermediate (60%) stenosis in a hypoplastic right coronary artery. Outpatient cardiac magnetic resonance (CMR) imaging showed no definite evidence of myocarditis. The clinical course and diagnostic findings favored myocardial injury secondary to the acute infection. Pembrolizumab rechallenge will therefore be attempted. *Case 2.* 60-year-old male smoker with type 2 diabetes mellitus and dyslipidemia, receiving pembrolizumab for metastatic melanoma of unknown primary, presented to the Emergency Department with exercise intolerance two weeks after his second cycle. Echocardiography revealed a dilated left ventricle with severely reduced systolic function (LVEF 17%, down from 44% before ICI initiation). Troponin was markedly elevated (hs-cTnI 419 ng/L), but the patient declined hospital admission. Empirical oral methylprednisolone (16 mg/day) was initiated for suspected ICI myocarditis, together with guideline-directed medical therapy (GDMT) for heart failure. During a subsequent admission, coronary angiography demonstrated severe three-vessel coronary artery disease. Methylprednisolone was discontinued and GDMT was further up-titrated. Outpatient stress echocardiography and CMR are planned. Our multidisciplinary cardio-oncology team will decide on further cancer therapy based on these results and the revascularization strategy.

Conclusion: Although a temporal association with immunotherapy, troponin elevation and worsening systolic function warrant prompt consideration of ICI myocarditis, these findings are not specific to immune-mediated cardiotoxicity. Infectious and ischemic mechanisms may mimic ICI myocarditis or coexist with it. Once an alternative cause is identified, excluding concomitant ICI myocarditis remains particularly challenging. An integrated approach is therefore essential, combining clinical context, multimodality imaging and coronary evaluation to guide individualized decisions on immunosuppression and continuation of immunotherapy.

RECEIVED:
October 24, 2026
UPDATED:
November 4, 2026

LITERATURE

1. Morad TT, Keykhaei M, Terraciano DA, Srivastava PK, Yang EH, Stein-Merlob AF. Management and Surveillance of Immune Checkpoint Inhibitor Myocarditis: Managing the Aftermath. JACC CardioOncol. 2026;8(5):483-502. https://doi.org/10.1016/j.jaccao.2026.09.003
2. Salem JE, Ederhy S, Zhang M, Bretagne M. Rechallenge After Immune Checkpoint Inhibitors Myocarditis: Evidence and a Practical Framework. JACC CardioOncol. 2026;8(5):503-506. https://doi.org/10.1016/j.jaccao.2026.05.009
3. Lyon AR, López-Fernández T, Couch LS, Asteggiano R, Aznar MC, Bergler-Klein J, et al; ESC Scientific Document Group. 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). Eur Heart J. 2022 Nov 1;43(41):4229-4361. https://doi.org/10.1093/eurheartj/ehac244