

ABSTRACT**A Re-Challenging Case**Walter Schiffer^{1,2}, Kathleen Zhang^{1,2}, Douglas Kyrrouac^{1,2}, Daniel Lenihan^{1,2}¹Washington University School of Medicine, St. Louis, MO 63110²Barnes-Jewish Hospital, St. Louis, MO 63110

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Am J Hosp Med 2020 Jan;4(1):2020.006 <https://doi.org/10.24150/ajhm/2020.006>**INTRODUCTION**

Immune Checkpoint Inhibitors (ICI) are associated with multiple cardiotoxic effects. Balancing adverse effects with anti-tumor response poses a challenge to treating advanced cancers. The safety of re-starting ICI therapy after an adverse event is unknown. We present the case of a 58-year-old man with stage IV melanoma ICI-related myocarditis and complete heart block (CHB).

CASE

A 58-year-old man with stage IV melanoma status-post cycle one of ipilimumab/nivolumab was admitted for new-onset shortness of breath. ECG showed new CHB, and his troponin I level was elevated to 2.8. He underwent left heart catheterization (LHC), which did not demonstrate significant coronary artery disease. A cardiac MRI showed no late gadolinium enhancement (LGE). Cardiac biopsy pathology showed myocarditis with positive PD-L1 positive immunostaining. The patient was managed with pulse-dose steroids for ICI-related myocarditis, with resolution of his complete heart block one month later. A permanent pacemaker was placed empirically in anticipation of resuming ICI therapy. Five months later, the patient was re-trialed with pembrolizumab.

He received 5 cycles before ICI therapy was discontinued due to tumor progression. He tolerated the therapy well without further serological or clinical evidence of additional cardiovascular adverse effects.

DISCUSSION

ICIs represent a class of chemotherapies that aim to invigorate tumor-infiltrating lymphocytes (TILs) against cancer by targeting PD-1, PDL-1, and CTLA-4, and have demonstrated effectiveness in multiple cancers, including melanoma and non-small cell lung cancer. However, ICIs may have multiple adverse effects on the heart, including myocarditis. Patients who develop myocarditis present with a troponin elevation and abnormal ECG, but may have a normal LVEF. Workup includes cardiac MRI, which may reveal LGE, though it did not in this case. A LHC is performed to rule-out coronary ischemia. Treatment relies on high-dose steroids. What remains unclear, however, is the potential ability to restart ICI therapy after the treatment of ICI-related myocardial toxicity, especially when these therapies represent the last line of treatment. In this case, the patient was successfully treated with steroids leading to a resolution of his arrhythmia and improvement in symptoms. He was able to restart ICI treatment with a second-line PD-1 without

recurrent cardiovascular complications. Interestingly, the patient's lymphocyte count decreased from a normal level of 2K/cumm at the start of ICI use to 0.2 K/cumm after steroid administration, suggesting a possible lack of immunologic reserve, and therefore an inability to mount an auto-immune response.

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