A Case of Immune Checkpoint Inhibitor Myocarditis Detected on Routine Troponin Monitoring

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Introduction

Immune checkpoint inhibitors (ICIs) are novel drugs that activate T cell-mediated anti-tumor response leading to improved cancer patient survival. Despite these benefits and their increased usage over the past decade (Figure 1), myocarditis can be a serious side effect of immunotherapy, ranging in clinical presentation from subclinical to fulminant. Although retrospective data suggests that elevated troponin is found in up to 94% of patients and is associated with worse CV outcomes, routine screening with troponin levels is not standard practice. Here, we present a case of ICI myocarditis detected on routine troponin monitoring.

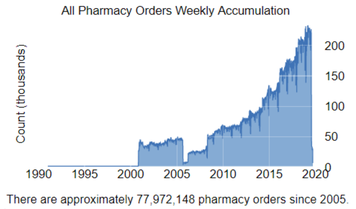

Figure 1. Total pharmacy orders of immunotherapy at the high-volume Stanford Cancer Center have increased dramatically since 2005.

History and Presentation

A 76-year-old male with stage III lung adenocarcinoma and no cardiac history received standard radiation/chemotherapy followed by initiation of the immune checkpoint inhibitor durvalumab (a PD-L1 inhibitor) 10 mg/kg biweekly (per standard of care – PACIFIC trial). Routine 10-week labs at fifth cycle of durvalumab showed a troponin of 1.232 ng/mL (ref <0.055 ng/mL), with no baseline for comparison. Patient had no signs of other autoimmunity. A repeat troponin one week later was 0.145 ng/mL. EKG showed no ischemic changes. The patient declined admission as he was asymptomatic and felt well. A transthoracic echocardiogram (TTE) detected a left ventricular ejection fraction (LVEF) of 56% and no wall motion abnormalities. A cardiac MRI detected abnormal delayed myocardial enhancement (DGE) in the basal anterolateral wall associated with subtle T2 hyperintensity, suggestive of myocardial edema.

One week later, his troponin prior to the sixth cycle of durvalumab was 10.394 ng/mL. He was admitted for coronary evaluation, although he remained asymptomatic. His EKG showed normal sinus rhythm at a heart rate of 78 bpm and no ischemic ST or T wave changes. A CT coronary angiogram showed no significant coronary artery disease (with calcium score of 0). A repeat TTE demonstrated LVEF 59% and subtle inferior/posterior wall hypokinesis.

Laboratory & Imaging Results

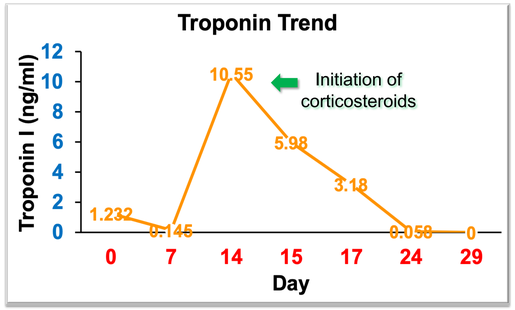

Figure 2. Troponin trend and treatment course.

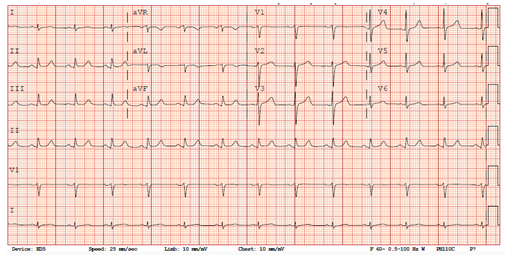

Figure 3. Electrocardiogram (EKG) on presentation showed normal sinus rhythm with HR 78 and no ischemic ST or T wave changes.

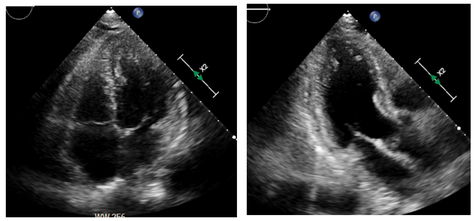

Figure 4. Echocardiogram apical four-chamber view (left) demonstrated normal left ventricular ejection fraction of 59%. Apical three-chamber view(right) showed subtle inferior/posterior wall hypokinesis.

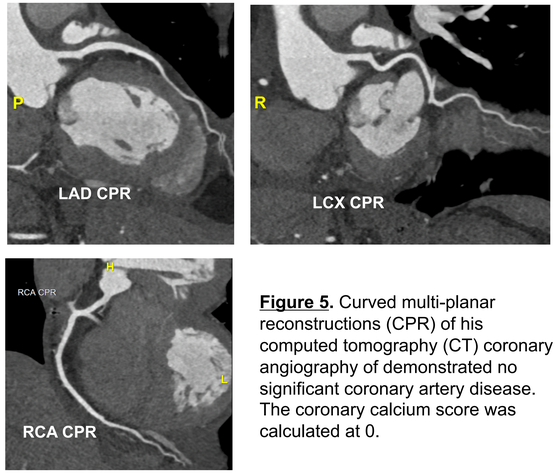

Figure 5. Curved multi-planar reconstructions (CPR) of his computed tomography (CT) coronary angiography of demonstrated no significant coronary artery disease. The coronary calcium score was calculated at 0.

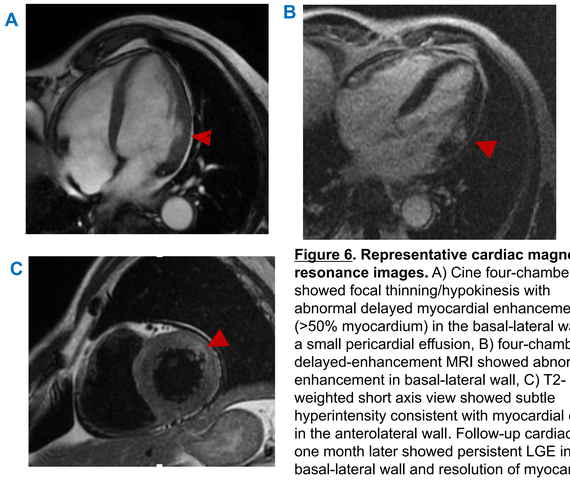

Figure 6. Representative cardiac magnetic resonance images. A) Cine four-chamber view showed focal thinning/hypokinesis with abnormal delayed myocardial enhancement (>50% myocardium) in the basal-lateral wall with a small pericardial effusion, B) four-chamber delayed-enhancement MRI showed abnormal enhancement in basal-lateral wall, C) T2-weighted short axis view showed subtle hyperintensity consistent with myocardial edema in the anterolateral wall. Follow-up cardiac MRI one month later showed persistent LGE in basal-lateral wall and resolution of myocardial edema and pericardial effusion.

Hospital Course

The patient was initiated on high dose corticosteroids. His troponin peaked at 10.666 ng/mL and down-trended to 5.842 ng/mL over 24 hours on prednisone 60 mg daily. He was discharged with a six-week oral prednisone taper with weekly labs.

Two months after discharge, he remained without recurrent disease off immunotherapy, with undetectable troponin (<0.017 ng/mL) and a follow-up cardiac MRI showing stable area of DGE with stable cardiac function.

Discussion

Significant cardiac biomarker elevations may be seen in patients receiving immunotherapy without overt clinical signs and symptoms. A high level of attention is required, given that the delayed initiation of steroids may lead to higher rates of MACE. Routine biomarker monitoring may detect cases of subclinical myocarditis with early imaging signs of myocardial dysfunction and improve cardiac safety for patients on immunotherapy.

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