# A RARE CASE OF FULMINANT IMMUNE CHECKPOINT INHIBITOR MYOCARDITIS

Chukwunonso Ezeani, MD; Gift Echefu, MD; Ifeoluwa Stowe, MD; Bryan Hathorn, MD

Baton Rouge General Internal Medicine Residency Program

Louisiana Cardiology Associates, Baton Rouge

Baton Rouge General

Internal Medicine Residency Program

Baton Rouge General

Internal Medicine Residency Program

## Introduction

Immune checkpoint inhibitors (ICI) Myocarditis is a rare adverse event, with a prevalence of about 0.04% and high mortality ranging from 25% to 50%.

There is limited data on diagnosis, effectiveness and duration of therapy. We present a case of pembrolizumab induced fulminant myocarditis.

## Case Description

A 41-year-old lady presented with substernal chest pain for a day, with nausea and vomiting. In the months prior to presentation, she was diagnosed with invasive right ductal carcinoma and received Carboplatinum and Paclitaxel. Afterwards, she was placed on Pembrolizumab. Echocardiogram pre-immunotherapy was normal.

Vital signs revealed bradycardia and hypotension and she had a thready and irregular pulse with an otherwise unremarkable physical exam. Labs (Table 1) revealed elevated troponin of 29.65 ng/ml and brain natriuretic peptide of 145 pg/ml. Electrocardiogram (EKG) showed sinus waves with bigeminy and T-wave inversions in the lateral leads (Figure 1). Repeat EKG an hour later showed marked sinus bradycardia with prolonged QT interval (Figure 2). Chest X-ray was normal. Due to concern for Non-ST elevation myocardial infarction, she underwent cardiac catheterization which showed normal coronary arteries. Hypotension however worsened despite aggressive fluid resuscitation with intravenous fluids and albumin so she was started on amiodarone and norepinephrine. Repeat labs showed hypomagnesemia of 1.4 mmol/L which was repleted. She subsequently went into ventricular tachycardia, remained hypotensive and was cardioverted with 200J in a synchronized fashion but had persistent wide complex tachycardia. She had a seizure activity, received intravenous lorazepam and was intubated.

Following intubation, she became more bradycardic, and atropine was given but she unfortunately suffered a cardiac arrest shortly afterwards and cardiopulmonary resuscitation (CPR) was initiated with several rounds of epinephrine, calcium, steroids and bicarbonate with subsequent return of spontaneous circulation (ROSC). Echocardiogram during resuscitation showed good ventricular squeeze with a questionable right heart dilation. She then received heparin due to suspicion for pulmonary embolism. She however became bradycardic again and had a second cardiac arrest with re-initiation of CPR. After multiple unsuccessful attempts, the patient expired within 12 hours of hospitalization. An autopsy was carried out and histology revealed diffuse lymphocytic myocarditis with myocyte hypertrophy.

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## Figures and Labs

| Parameters | Value on presentation | Reference Range |
|---|---|---|
| Troponin 1 | 29.65 | 0.00-0.03 ng/mL |
| AST | 139 | 10-58 U/L |
| BNP | 145 | 15- 111 pg/ml |
| Magnesium | 1.4 | 1.6-2.6 mg/dL |
| Glucose | 109 | 70-100 mg/dL |

Table 1: Lab values

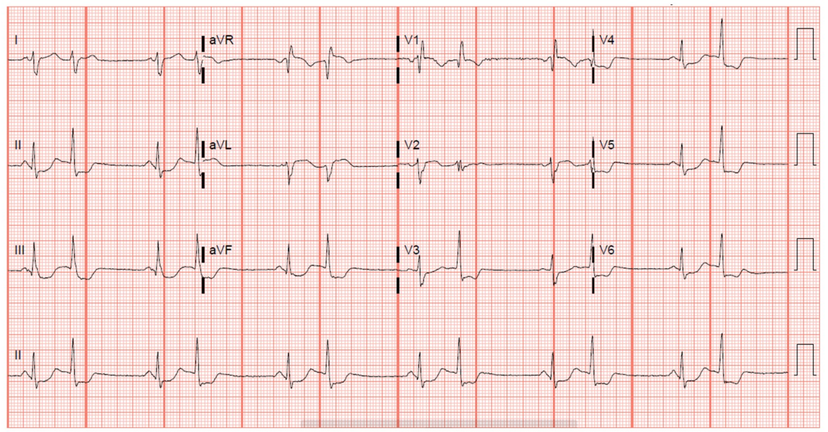


Figure 1: Sinus bradycardia with Bigeminy and T wave inversions

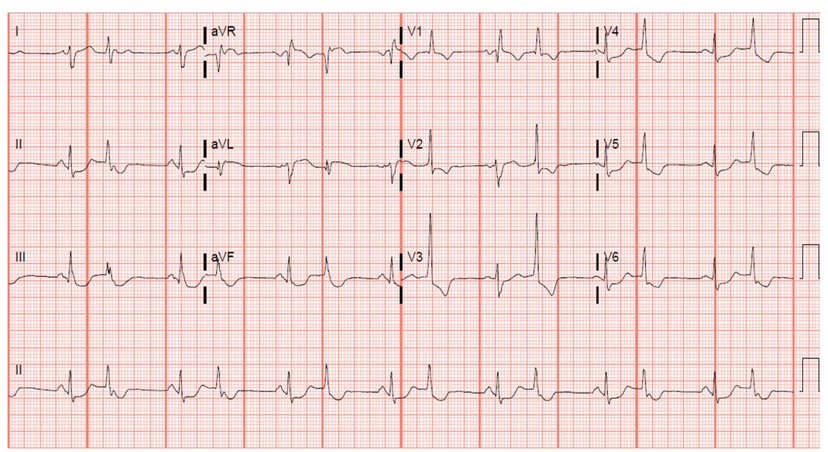


Figure 2: Worsening sinus bradycardia with prolonged QT interval

## Discussion/Conclusion

ICI myocarditis has non-specific clinical presentation and poses diagnostic and therapeutic challenges for clinicians. Median time from symptom onset to death is 32 days, which is remarkably different from this case where death occurred within 12 hours of presentation. Myositis was frequently reported in a study of patients who had fatal ICI myocarditis, however this was not present in our patient. Our patient was significantly younger than the mean age of 72 years that was noted in a recent meta-analysis.. Symptoms have been documented to occur within 3 days to one year after initiation of immunotherapy.

New onset acute coronary syndrome or heart failure symptoms should raise strong suspicion for ICI myocarditis in patients who are currently on or recently completed immunotherapy. This is essential as clinical deterioration can occur within hours of presentation as in our patient. Cardiac Magnetic Resonance with late gadolinium enhancement is helpful in diagnosis and will show edema and inflammation.

High dose steroids, Infliximab and intravenous immunoglobulin have been used for treatment. Studies show a mean duration of 5 days from onset of symptoms to initiation of therapy due to a delay in diagnosis. This challenge may have contributed to the high mortality of this condition.

While immune checkpoint inhibitors are very effective, their adverse effects can be devastating. There is a need for increased awareness to ensure early diagnosis and initiation of treatment.

## References


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