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Case Report

Immune Checkpoint Myocarditis from Adjuvant Treatment of Melanoma

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ABSTRACT

Immune checkpoint inhibitors (ICIs) are effective therapy for many metastatic cancers and are now being used as adjuvant treatment for many stage III cancers to reduce the high risk of reoccurrence. ICIs activate a patient's own T-cells to fight cancer, but in some cases, immune-related adverse events (irAEs) with inflammation of many organs can occur. Rare cases of myocarditis have been reported. More data is needed to improve our ability to monitor, diagnose and treat irAEs.

Introduction

Immune checkpoint inhibitors have shown great promise in improving cancer outcomes in a wide range of malignancies. These drugs work by preventing tumor cells from binding to host immune system checkpoint proteins, ultimately leading to tumor cell death. Immune checkpoint inhibitors, however, have also been associated with a variety of immune-related adverse events that can involve the lungs, skin, liver, and many other organ systems. Recent studies have also highlighted an increasing awareness of autoreactive T cell-mediated inflammation-causing myocarditis early after ICI exposure [1, 2]. Here, we present a case of a patient who developed myositis and presumed myocarditis after receiving one dose of pembrolizumab (Keytruda®).

Case Report

70-year-old male with a past medical history significant for obesity (body mass index of 47), coronary artery disease with prior stenting for angina, hypertension, hyperlipidemia and stage III melanoma treated with resection and received one dose of adjuvant pembrolizumab. Three weeks after his infusion of pembrolizumab, he presented with a several-day history of diffuse joint pain which was worse in the lower extremities. The lower extremity discomfort was bothersome to the point simple activities like getting up to move around his house was painful and he avoided it. From a cardiac standpoint, he noted feeling that he could not take a deep breath at rest or with exertion but no angina, edema, orthopnea, paroxysmal nocturnal dyspnea. Pertinent review of systems included no fevers, chills, rashes, change in urine color or diarrhea. Hours prior to hospital admission, he took steroids which improved his muscle aches and breathing. During his admission, he was found to have a Grade 3 transaminitis, peak creatinine kinase (CK) of 13,600 Units/L and peak high sensitivity (hs)-troponin of 2,700 ng/L. He was treated with 1g IV Solumedrol for three days with a slow taper, as well as two sessions of plasma exchange. Electrocardiogram and telemetry were unremarkable. Transthoracic echocardiography was limited by poor acoustic windows but revealed grossly normal biventricular function and trivial pericardial effusion. He was unable to tolerate cardiac MRI due to dyspnea when supine. At discharge, CK had also improved to 1,089 Units/L and troponin was 208 ng/L. TTE performed one week after discharge was stable and the patient had symptomatically improved. He received one dose of abatacept 500mg ten days after discharge and was on a steroid taper.

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Unfortunately, approximately four weeks after discharge, he was admitted to another institution for severe shortness of breath. He was found to be volume overloaded and had a new oxygen requirement of 2 liters. Lab abnormalities at this time included: CK 998 Unit/L, hs-troponin 624 ng/L, NT-proBNP 929 pg/L, sodium 121 mg/dL, Cr 0.5 mg/dL, AST 85 Units/L, ALT 202 Units/L. The patient was re-started on Solumedrol and a diuretic regimen. Three days into this admission, the patient became progressively more confused and was found to have hypoxic, hypercapnic respiratory failure and was started on BiPAP to maintain adequate saturation. Given his increasing care needs, the patient was transferred to a tertiary care center. Upon transfer, labs were notable for leukocytosis, acute kidney injury with creatinine of 1.9 mg/dL, AST 42 Units/L, ALT 81 Units/L, CK 815 Units/L, hs-troponin 98 ng/L, BNP 214 pg/L and an ABG with a mixed metabolic acidosis. The patient was subsequently placed on BiPAP at 40%, with improvements in his oxygenation status. Electrocardiogram obtained at that time showed new atrial fibrillation with a rapid ventricular response which required an amiodarone drip but was otherwise was free of any new conduction abnormalities. Plain film of the chest showed a left basilar opacity with pleural effusion. Transthoracic echocardiography once again had very poor windows due to the patient's body habitus and was not diagnostic. Within 48 hours, the patient was weaned to a nasal cannula and a slow steroid taper was initiated. The following day, labs were notable for moderate improvement in CK to 386 Units/L and hs-troponin to 54 ng/L. However, the patient developed rapidly progressive confusion and was found to be hypercapnic with pCO_2 78.8. BiPAP was reinitiated and the patient's ABG normalized, but he remained persistently confused in the setting of CO_2 narcosis, suffered a PEA arrest and unfortunately passed away despite aggressive resuscitative attempts.

Discussion

This case highlights the importance of close monitoring of patients receiving checkpoint inhibitors and the need for robust research in the field of immune-related adverse events. Currently, there are no clinical guidelines for routine monitoring for ICI-myocarditis, diagnosis or treatment. Myositis is associated with concurrent myocarditis, as was seen in this case [1]. Extrapolating from expert consensus on adjudicating for myocarditis events in clinical trials, this patient had possible myocarditis [2]. Steroids are the mainstay of immune-related adverse events, although additional immunosuppression can be used like infliximab, rituximab and mycophenolate mofetil. In this case, hs-troponin was the only evidence of myocardial injury due to an inability to adequately image the patient secondary to body habitus. Given continued hs-troponin elevation despite plasmapheresis, the decision was made to give the patient abatacept, a checkpoint protein agonist, in an effort to halt checkpoint mediated myocarditis [3]. More data is needed on how we should monitor for irAEs in patients treated with ICIs especially as immunotherapy is expanded to treat stage III cancers.

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