The Life Threatening Triad of Opdivo: Immunotherapy Induced Overlap Syndrome

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Abstract

Immune checkpoint inhibitors (ICI) are monoclonal antibodies that target immune checkpoint inhibitory receptors. They have revolutionised cancer treatment but can be associated with a wide range of adverse side effects. Rarely, they can be associated with the triad of myositis, myasthenia gravis, and myocarditis or overlap syndrome. These effects can be life-threatening and occur typically in the first two months of starting the immune check point inhibitors. Prompt recognition and early intervention are needed to treat these potentially life-threatening conditions. This case highlights the rare side effect and early recognition of overlap syndrome in a patient that was recently started on opdivo. 69 year old male with past medical history of melanoma presented for rash and difficulty breathing for the last couple of days. In regards to his cancer history the patient states that he had recently started opdivo 3 weeks ago, does follow with oncologist, and did have the melanoma removed recently. On initial presentation, the patient had gone to an urgent care where he was provided steroids and told to come to the ER for further evaluation. Patient continued to have worsening hypoxia while in the hospital with an ABG that had shown ph of 7.41, pco2 of 56.0, po2 is 63. Throughout the hospital course the patient developed worsening hypoxia and increased oxygen requirements leading to BiPAP therapy. Although the patient originally had a diagnosis of bronchitis due to productive cough and upper respiratory symptoms the progression of hypoxia and worsening dyspnea made the suspicion for immune check point induced pneumonitis high. Patient also had an elevated CK of 1,716 that had improved to 882 then to 318 demonstrating acute myositis at that time. His labs was also remarkable for elevated transaminases as well as elevated troponins and was diagnosed with an NSTEMI at that time. Although the patient was diagnosed with an NSTEMI initially by cardiology, the possibility of ICI induced myocarditis was high. Cardiac MRI was ordered and had not shown obvious cardiac myositis indicating that this patient's diagnosis was caught early enough to where the imaging would not pick up the organ involvement. With the worsening muscle weakness throughout the day and PFTs performed this admission that had shown a restrictive pattern, this supported a diagnosis of myasthenia gravis with restrictive lung disease from opdivo. During this admission the patient was started on solumedrol therapy as well as IVIG for the myasthenia gravis and myositis. NIF score was also calculated this admission which had shown a NIF -35 and VC 1.8L. Acetylcholine receptor blocking antibody positive at 41%, r requiring mestinon and an additional round of IVIG. Upon literature review, studies have shown that the acetyl chole receptor blocking antibody that was positive at 41% could be a low normal positive in the setting of an opdivo induced myasthenia gravis. With this treatment, adequate oxygenation, and close monitoring the patient continued to improve until they were deemed medically safe for discharge. Current literature states that this overlap syndrome is associated with high mortality and morbidity rate. However, this case highlights the early recognition and treatment that can be provided to reduce the overall likelihood of death from an opdivo induced overlap syndrome.