A Case of Nivolumab-Induced Myositis

Introduction

The May 2016 issue of ***The Oncologist*** summarizes U.S. Food and Drug Administration approval for nivolumab in non-small cell lung cancer [1]. In response, we present a case of nivolumab-induced myositis, an unlisted side effect that has been reported only once previously. Nivolumab (Opdivo) is a monoclonal antibody classified as an immune modulator. It binds to programmed cell death-1 (PD-1) and blocks the PD-1 pathway, allowing immune cells to attack a tumor efficiently [2].

Case Presentation

The patient is a 75-year-old female with a medical history of diabetes, hypertension, renal insufficiency, myositis with elevation of creatine phosphokinase (CPK) to 9,987 U/L from simvastatin use in 2010, hyperlipidemia, depression, arthritis, and melanoma on the right leg, which was diagnosed and excised in 2006. In 2015, her dermatologist recommended rebiopsy of the right-leg lesion. Pathology from the right leg showed invasive melanoma. This was re-excised with sentinel lymph node biopsy in the right inguinal region. The biopsy of the right lower extremity showed malignant melanoma with a Clark level IV and Breslow depth of 7.5 mm. The sentinel lymph node contained metastatic malignant melanoma measuring 1.7 cm. *BRAF* mutation was not detected. A positron emission tomography scan revealed disease in her supraclavicular, retroperitoneal, and pelvic lymph nodes. Because of this metastatic adenopathy, systemic treatment was warranted. The patient's renal function (creatinine 2.7) limited treatment options. Nivolumab was started at 3 mg/kg every 2 weeks. After her second dose, the patient developed severe muscle pain, difficulty breathing, shortness of breath, and an inability to lift her legs. The patient had a similar response to Simvastatin in 2010. She presented to the emergency room. A lung ventilation/perfusion scan revealed a low probability for pulmonary embolism, a chest x-ray showed no active disease, and an electromyography scan showed mild myopathic changes in proximal muscles. The CPK was elevated to 1,180 U/L (normal = 15–200 U/L). The patient was not taking any medications known to cause myositis, and rheumatologic workup was negative for autoimmune disease. Nivolumab was discontinued, and the patient was started on prednisone. After these interventions, the patient's symptoms subsided, and the CPK normalized after 8 days.

Discussion

Given the initiation of nivolumab, a drug-induced myositis was the most likely cause of the patient's symptoms. As a new medication, a complete understanding of the side effects of nivolumab is essential. Nivolumab causes immune-mediated side effects such as pneumonitis, colitis, hepatitis, and hypothyroidism. Myositis from nivolumab has been reported only once in a case study in which the patient was concurrently taking atorvastatin [3]. HMG coenzyme A (Co-A) reductase inhibitors or statins are known to cause myotoxicity that is likely specific to the HMG Co-A reductase pathway [4]. Pembrolizumab has a mechanism similar to that of nivolumab and is also used to treat melanoma. Pembrolizumab caused rhabdomyolysis in trial phase, and the adverse effects of pembrolizumab include myositis [5]. We report a case of myositis in response to nivolumab. Although we report on an overlapping myotoxicity, it is currently not known whether there is a common mechanism for myositis with pembrolizumab that would preclude its use.

Author Contributions

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Disclosures

The authors indicated no financial relationships.

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