

Abstract Form

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Project Title:	“Multifocal Pneumonia: Checking for Checkpoint Complications”

Research Category (please check one):

<input type="checkbox"/>	Original Research	<input checked="" type="checkbox"/>	Clinical Vignette	<input type="checkbox"/>	Quality Improvement	<input type="checkbox"/>	Medical Education Innovation
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Abstract

Case Description: 70-year-old female with history of renal cell carcinoma with hepatic and pulmonary metastases, diabetes mellitus, depression, and hypothyroidism presented to the ED with progressive shortness of breath, cough, and fatigue for 1 week. She was recently started on monthly nivolumab infusions with the last treatment being 5 days prior to presentation. On exam, the patient was afebrile with heart rate 100 bpm, respiratory rate 20/min., initial oxygen saturation 88% on room air, which improved to 94% after being placed on supplemental oxygen. She had coarse breath sounds with scattered rhonchi throughout. CBC had normal WBC with left shift, Hb of 8.5, Hct of 25.7, and platelets of 914K. Serum sodium was 126, potassium 5.5, bicarbonate 16, anion gap 12, BUN 66, serum creatinine 1.6, and alkaline phosphatase 195. Procalcitonin was 11.2 ng/ml. Respiratory viral panel (including COVID-19, RSV, Influenza A/B, Parainfluenza 1-4, Human metapneumovirus, Rhinovirus, Adenovirus) was negative. Hepatitis panel was also negative. EKG showed right bundle branch block without ischemic changes. CT chest without contrast revealed bilateral patchy consolidations with upper lobe predominance and bilateral hilar and pericardial lymphadenopathy. The patient was started on broad spectrum antibiotics including atypical coverage, given IV fluids and sodium-zirconium cyclosilicate, and admitted for further management of severe sepsis. ID was consulted and recommended continuation of antibiotics along with further diagnostic tests of Legionella Ag, Histoplasma Ag, Aspergillus Ag, Cryptococcus Ag, Coccidioides Ab (IgM/IgG), all of which were found to be negative. A sputum specimen could not be produced despite induction. Blood cultures were negative. The patient’s respiratory status continued to decline with increasing oxygen requirements. A repeat CT chest with contrast showed worsening bilateral infiltrates and consolidation consistent with multifocal pneumonia and increased right pleural effusion. CTPA was negative for PE. BAL specimens were negative for Aspergillus Ag, *P. jiroveci* PCR, M Tb PCR. bacterial and fungal cultures, KOH smear, and AFB stains. After extensive multidisciplinary discussion, antibiotics were discontinued and the patient was started presumptively on methylprednisolone 60 mg BID for suspected acute interstitial pneumonitis secondary to nivolumab. The patient was noted to have significant improvement with decreased oxygen requirement and her steroids were able to be tapered. Goals of care and hospice were also discussed with the patient, however she wished to continue with intensive medical treatment and was discharged home on a continued steroid taper and supplemental oxygen and to follow up closely with her primary care physician, oncologist, and pulmonologist.

Discussion: Over the past decade, the development of novel immunotherapy treatments has led to improved prognosis in patients with advanced malignancies. Specifically, immune checkpoint inhibitors (ICIs), which act as antibodies against programmed cell death receptor 1 (PD-1) and programmed cell death ligand 1 (PD-L1), have become widely available for use. Although ICIs have demonstrated clinical benefit, they also have been associated with immune-related adverse events. Our patient with metastatic renal cell carcinoma had worsening shortness of breath 5 days after receiving nivolumab infusion. Although uncommon, pneumonitis can be a severe or even fatal complication of ICI treatment. Onset of pneumonitis from initiation of ICI therapy varies widely (9 days to 19 months), however has been noted to occur earlier for those treated with combination versus single agent therapy. Clinicians should suspect immune-mediated pneumonitis in patients on active treatment with ICI who present with new or worsening cough, shortness of breath, dyspnea on exertion, and/or oxygen requirement.

Conclusion: As ICI use becomes prevalent in cancer treatment, clinicians should be aware of potential adverse reactions. This case highlights the importance of prompt recognition of nivolumab-induced acute interstitial pneumonitis as well as that of a multidisciplinary team approach to management of complex patients with advanced malignancies on ICIs.