

Pembrolizumab Induced Pneumonitis: Fatal Despite Treatment

Naif Hindosh MD, Giorgi Gelagutashvili MD

SLUHN Anderson campus

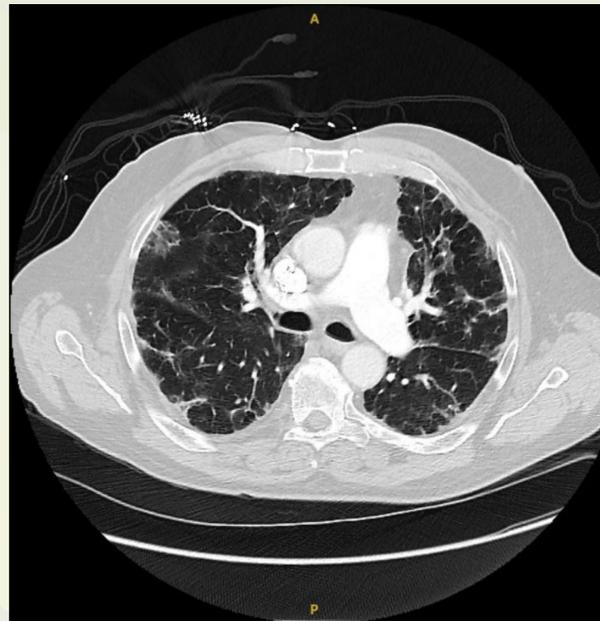
Introduction

- Pembrolizumab is a monoclonal antibody that is used as an immunotherapy for solid organ and hematologic malignancies.
- Acts by blocking the PD-1/PD-L1 pathway thereby eliminating the inhibitory effect of the immune response.
- This action may result in immune-mediated adverse reactions including pneumonitis.

Case presentation

- A 63-year-old male with past medical history significant for metastatic carcinoma of unknown primary and liver metastasis presenting with worsening hypoxia.
- One month prior to presentation, he was diagnosed with drug-induced pneumonitis secondary to pembrolizumab and started on prednisone taper. Pembrolizumab was discontinued.
- He was afebrile on admission. Physical exam was notable for coarse breath sounds with no signs of volume overload. A CT angiography of the chest was negative for pulmonary embolism, however showed extensive worsening multifocal bilateral ground-glass opacity. COVID-19 PCR was negative and other infectious processes were excluded.
- He required 6L supplemental nasal canula oxygen initially, however this quickly escalated to the need for high-flow oxygen. He showed no improvement despite broad-spectrum antibiotics, high dose IV methyl-prednisone, infliximab, and IVIG.
- The patient declined intubation, was transitioned to comfort care and passed away.

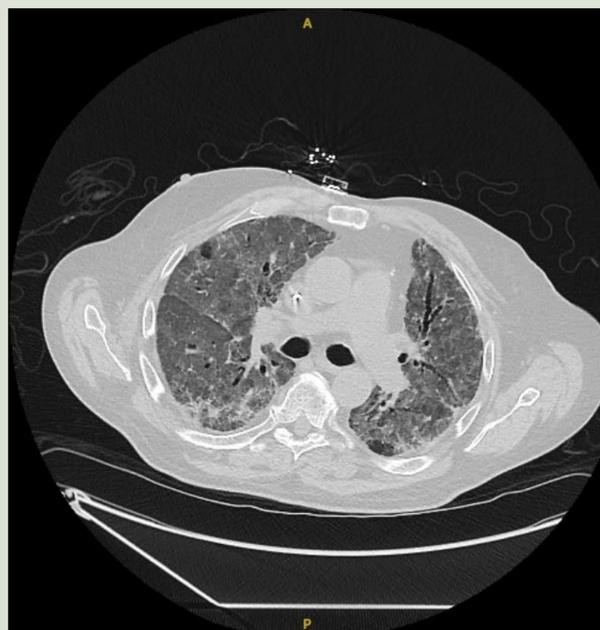
CTA-PE-chest. Initial diagnosis:



CTA-PE-chest 10 days before the patient passed away:



CT chest wo-contrast 4 days before the patient passed away:



Discussion

- Pneumonitis accounts for less than 5% of adverse reactions of PD-L1 inhibitors and can be life-threatening.
- The presentation is usually non-specific and may mimic other pulmonary conditions. Factors such as a history of COPD, smoking, and prior thoracic radiation have been linked to increased incidence of pneumonitis.
- Studies have shown that pneumonitis is not dose dependent.
- A cross-sectional CT scan of the chest is a better tool for diagnosis. Most common radiographic findings are peripheral ground-glass or consolidative opacities. A grading system has been used for management.
 - Grade 1 is described by radiographic findings with no symptomology and is managed by delaying immunotherapy and repeating imaging studies every 3 weeks.
 - Grade 2 correlates to mild breathlessness and cough and is managed by holding the causative agent with consideration for hospital admission for IV methyl-prednisone, followed by 1 month prednisone taper.
 - Grade 3-4 is defined by severe hypoxia and life-threatening respiratory failure requiring critical care admission with or without ventilatory support.
- Permanent discontinuation of the drug is recommended, and treatment usually includes IV methyl-prednisone with steroid taper over 6 weeks.
- Studies have shown utility with immunosuppressants such as infliximab, mycophenolate mofetil, cyclophosphamide, and IVIG if no improvement achieved within 48 hours of steroid therapy.

References

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