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.

Introduction

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.

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