

OBJECTIVES

1. Associate immune checkpoint inhibitors with related neurological complications .
2. Maintain a high clinical suspicion for immune checkpoint inhibitor related complications in patients on these medications.

INTRODUCTION

This is a 60-year-old-man with squamous cell carcinoma of the left lip status post resection in 2008 and recurrence in 2020 to left cranial nerve (CN) V status post chemotherapy and radiation. In 2022, progressive CN V involvement was treated with pembrolizumab and radiosurgery. In 2023, he developed vertigo, gait instability, and bilateral lower extremity numbness.

He had outpatient Magnetic resonance imaging (MRI) brain which showed T2 hyperintensity and enhancement of the left extraocular muscles. At the time, the concern was these findings were due to further progression of his underlying cancer and so he was continued on pembrolizumab treatment.

Over the following 3 months, his symptoms progressed, and he developed bilateral lower extremity weakness, urinary retention, dysphagia, left eye ptosis, and ophthalmoplegia. He presented to our hospital and neurology was consulted for his case.

CASE

He had a MRI brain and orbits performed which showed new smooth enhancement of the right cranial nerves VII and VII, left Cranial nerves III, IX, and X, and progressive abnormality of extraocular muscles. His MRI spine demonstrated smooth enhancement of thoracic nerve roots and dorsal cauda equina. The smooth enhancement seen on MRI was felt to represent and inflammatory rather than a malignant process. To further disseminate this, a lumbar puncture was performed which showed lymphocytic pleocytosis (16.7 nucleated cells), elevated protein (243), and normal glucose. CSF paraneoplastic antibody panel and flow cytology were negative. Electromyography showed multilevel lumbosacral radiculopathies without features of a demyelination or myopathic process.

He was diagnosed with multiple cranial neuropathies and polyradiculoneuropathy secondary to an immune response. His last dose was one month prior to admission. Immunotherapy was initiated. He received a course of high dose IV steroids and intravenous immunoglobulin (IVIg). He had incomplete clinical improvement. He was discharged home on oral prednisone. Over the following 1-2 weeks, his now profound neurologic deficits continued to progress, including dysphagia, limiting his ability to maintain adequate nutrition. He was readmitted to the hospital and his immunotherapy was escalated. He required ICU care due to aspiration pneumonia needing Zosyn and pressors. While he was admitted his high dose IV steroid regimen was repeated. Seven cycles of plasmapheresis (PLEX) were performed. Rituximab was initiated. He did not have significant clinical improvement, required gastric tube placement, and was discharged to acute inpatient rehab with a plan for weekly treatments of high dose IV steroids and IVIg. Rituximab was continued. Pembrolizumab was held indefinitely.

He was admitted to inpatient rehab and after 6 days, he did not notice any improvement in his ability to walk, his ability to swallow, or his ability to talk. He then ultimately decided to pursue at home hospice and passed two weeks later.

DISCUSSION

First approved in 2011, ICIs are an increasingly popular and effective tool in the treatment of cancer. Pembrolizumab is an immune checkpoint inhibitor (ICI) used to treat cancer¹. An estimated 1-6% of patients who receive ICIs will have neurologic immune-related adverse events². Current practice is to stop ICIs and initiate immune therapy which could include steroids, IVIg, PLEX, and/or immunosuppressant agents. There are no official guidelines on how to treat complications, monitor progress, and when to escalate/deescalate therapy². With increased use, more patients will experience neurologic side effects and so this must be in the differential diagnosis when patients develop new or progressive neurologic issues. More research is needed to understand the pathogenesis of neurologic complications, better screening to predict who is at risk of them, and how to effectively identify, treat, and monitor the complications if they occur³.

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