

PD-1 Inhibitors and Myasthenia Gravis Like syndrome.

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Abstract

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INTRODUCTION

- Program cell death 1 (PD-1) receptors are trans-membrane proteins on the surfaces of T-cells that interact with program death-ligands (PD-L) on somatic cells.
- PD-1 inhibitors have been used in treatment of advanced cancers like non-small cell lung cancer, metastatic melanomas, solid tumors and head/neck cancers.
- Due to PD-1 inhibitors blunting self-regulating immune responses, several immune-related adverse events (irAEs) have been linked with their usage.
- Reported neurologic adverse effects include dysphasia, tremors, ataxia, paresthesia's, paresis and others.
- We report 2 cases of Myasthenia Gravis like syndrome associated with PD-I inhibitors.

CASE PRESENTATIONS

- Case 1. 86 year old Male – PMH: Stage IV lung adenocarcinoma with hepatic & cervical spine metastases. Previously received Carboplatin and Pemetrexed.
- Patient switched to Nivolumab, (first infusion was 40 days prior to hospitalization and the third infusion occurred 10 days prior to admission).
- Patient presented to the ED with 1-week history of bilateral ptosis, right eye more than the left; dysphagia, neck weakness, and generalized fatigue, reflexes symmetric bilaterally.
- MRI Thoracic Spine revealed T8 mass like lesion likely metastatic from adenocarcinoma. MRI Brain, LP CSF analysis, EGD, & Anti-Muscle specific kinase [MuSK] and Acetylcholine antibodies and receptor antibodies were all negative.

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- Suspicion arose for Myasthenia Gravis like syndrome when he continued to develop worsening dyspnea, tachypnea and weakness.
- Treatment: Mestinon, Plasmapheresis, followed by IVIG 0.4g/kg for 5 days daily and then Solu-Medrol 500mg IV BID with clinical improvement.
- Case 2. 77 year old Male – PMH: T3aN0M0 Urothelial carcinoma which required open surgery and debulking.
- Two months following surgery, the patient received his first cycle of Pembrolizumab.
- Patient presented in the outpatient setting for emergent evaluation by Neuro-Oncologist 13 days following the infusion. Patient had generalized myalgia, arthralgia, diplopia while driving, left ptosis, cervical neck pain disabling patient from maintaining his neck upright with associated bilateral upper extremities weakness.
- Diagnostic studies revealed increased liver transaminases and mild leukocytosis. MRI Brain and Spine were non-revealing. Anti-Muscle specific kinase [MuSK] and Acetylcholine antibodies and receptor antibodies were all negative.
- Treatment: Mestinon, Solu-Medrol, and IVIG 0.4g/kg for 5 days infusions with clinical improvement.

DISCUSSION

- PD-1 inhibitors can cause various neurological complications.
- We report 2 cases with a novel complication of PD-1 inhibitor therapy: Myasthenia Gravis Like syndrome.
- The exact mechanism of Myasthenia Gravis Like syndrome is not well understood, however a likely explanation are antibodies that affect the neuromuscular junction.
- For patients, undergoing PD-1 inhibitor therapy, presenting with progressive weakness, ptosis, dyspnea, etc., Myasthenia Like syndrome should be considered.
- Treatment with Plasma Exchange, high dose steroids and IVIG can be effective treating these patients.

CONCLUSIONS

- Rapid recognition of Myasthenia Gravis Like syndrome in patients receiving PD-1 inhibitors can improve patient outcome.

PD-1 Inhibitors and Myasthenia Gravis Like Syndrome

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- PD-1 inhibitors have been used in treatment of advanced cancers like non-small cell lung cancer, metastatic melanomas, solid tumors and head/neck cancers.
- Due to PD-1 inhibitors blunting self-regulating immune responses, several immune-related adverse events (irAEs) have been linked with their usage.
- Reported neurologic adverse effects include dysphasia, tremors, ataxia, paresthesia, paresis and others.
- We report 2 cases of Myasthenia Gravis like syndrome associated with PD-1 inhibitors.

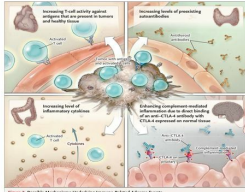


Figure 1. Possible Mechanism Linking Immune-Related Adverse Events. The mechanisms that result in immune-related adverse events are still being elucidated. Some general mechanisms include: increased T-cell activity against dendritic cells and subsequent immune response; increased dendritic cell activity against T-cells and subsequent immune response; increased dendritic cell activity against T-cells and subsequent immune response; increased dendritic cell activity against T-cells and subsequent immune response.

Reference: https://resident360.meds.org/content_item/side-effects-of-immune-checkpoint-blockade

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Discussion

- PD-1 Inhibitors can cause various neurological complications.
- Neurological side effects include tremors, dysarthria, ataxia, paresis and paresthesia's.
- We report 2 cases with a novel complication of PD-1 inhibitor therapy: Myasthenia Gravis Like syndrome.
- The exact mechanism of Myasthenia Gravis Like syndrome is not well understood, however a likely explanation are antibodies that affect the neuromuscular junction.
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