# Benign form of Myasthenia Gravis after Nivolumab treatment

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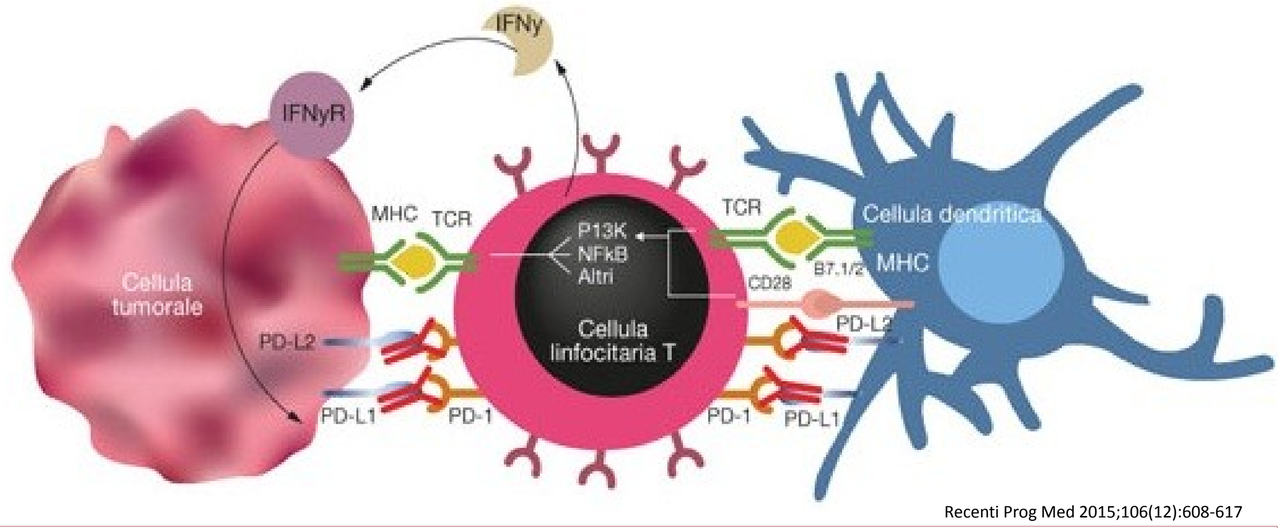
**Background: Myasthenia gravis (MG) is an autoimmune disease caused by antibodies against neuromuscular-junction. Nivolumab is a monoclonal antibody enhancing immune response against tumors by blocking inhibitory signals of cytotoxic T-lymphocyte antigen-4 and programmed cell death-protein-1 pathways (1). We report a case of a patient with lung adenocarcinoma developing iatrogenic MG after nivolumab treatment.**

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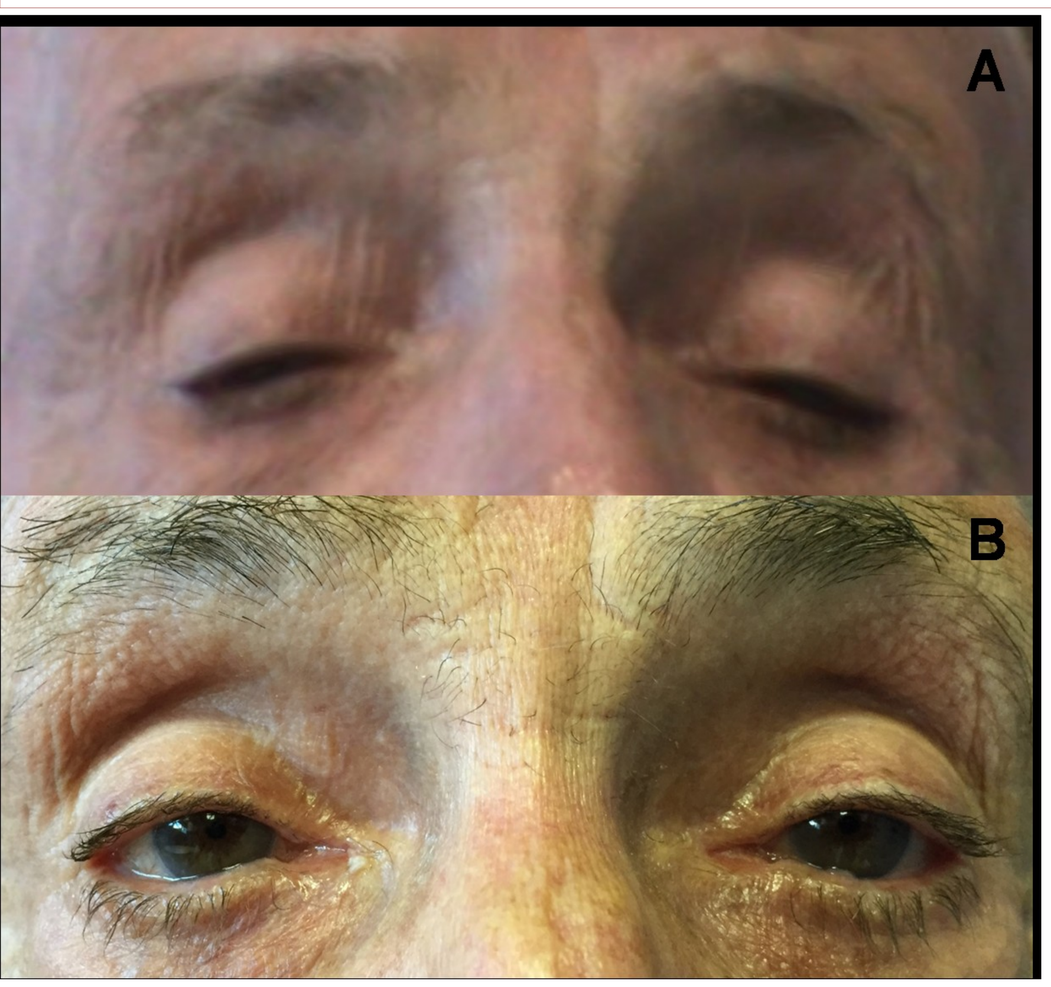


**Case Report:**

**A 81-year-old man with a two-year history of stage IV lung adenocarcinoma, refractory to three lines of chemotherapeutic drugs, started nivolumab 240 mg every 2 weeks. Following the third cycle of nivolumab administration, patient complained of ptosis and dysphonia. Neurological examination showed bilateral ptosis (Fig. A) without diplopia, nasal speech and strength of 4/5 in proximal muscles of four limbs. Single fiber electromyography of orbicularis oculi documented an increased jitter (mean jitter: 36 µs; pairs with abnormal jitter: 15%). Anti-acetylcholine receptor antibodies (a-AChR) were 0.40 nmol/L. Nivolumab was discontinued and patient treated with prednisone 50 mg daily, with clinical improvement 2 weeks after nivolumab withdrawal (Fig. B).**

**Discussion: Two fatal cases, describing the nivolumab-MG association, have been reported (2,3). Patient with lung cancer developed MG, after starting ipilimumab and nivolumab therapy (2). He was treated with prednisone 90 mg daily and he underwent plasmapheresis followed by intravenous immunoglobulin, with fatal exitus. The role of nivolumab as trigger of MG had not been established. Hence, ipilimumab-induced MG has already been documented. In the other reported case, a patient with metastatic melanoma developed MG, hepatitis and rhabdomyolysis after nivolumab administration (3). She complained of dyspnea as initial MG symptom. She was treated with prednisolone 2 mg/kg without improvement; immunoglobulin therapy was declined by relatives and patient died. To our knowledge, our report is the second case of MG induced by monotherapy with nivolumab and the third-one considering the association nivolumab-ipilimumab. Ocular symptoms, dysphagia, dysphonia and dyspnea should be researched in oncologic patients under treatment with nivolumab, as red flags of MG. a-AChR and neurophysiological tests are recommended in these patients. Therapeutic approach remains controversial. In all three cases, including our report, nivolumab withdrawal had been performed, in association with oral prednisone ranging from 50 to 90 mg daily or intravenous prednisolone. Plasmapheresis was performed in patient 1, whereas intravenous immunoglobulin was administered in patient 1 and recommended in patient 2. In our case nivolumab withdrawal and oral prednisone were sufficient to stop the evolution of the disease.**

**Conclusion: This is the first study reporting a benign form of nivolumab-induced MG with clinical improvement after steroid treatment.**

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## References

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