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Case Report
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Exceptional Occurrence of Amyotrophic Lateral Sclerosis Under Anti-PD-1

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Abstract

We report the exceptional observation of a patient treated with Nivolumab for a melanoma who developed amyotrophic lateral sclerosis. In the literature, ALS has only been reported once as an adverse effect of ICIs.

Over the past decade, cancer immunotherapy with Immune Checkpoint Inhibitors (ICIs) has significantly improved the outcome of many malignancies. However, with the broad use of ICIs, neurological immune related Adverse Events (irAE) are increasingly recognized. Myositis are the most frequent neurological complication, followed by peripheral neuropathies, myasthenic syndrome, encephalitis, cranial neuropathy, central nervous system demyelinating disease/ myelopathy, and aseptic meningitis.

Despite the few cases described, it is important to think of ALS when phonation and swallowing disorders appear under immunotherapy.

Keywords: Immunotherapy; Immune checkpoint inhibitor; Amyotrophic lateral sclerosis; Melanoma

Introduction

Over the past decade, cancer immunotherapy with Immune Checkpoint Inhibitors (ICIs) has significantly improved the outcome of many malignancies. However, with the broad use of ICIs, neurological immune related Adverse Events (irAE) are increasingly recognized. Myositis are the most frequent neurological complication, followed by peripheral neuropathies, myasthenic syndrome, encephalitis, cranial neuropathy, central nervous system demyelinating disease/ myelopathy, and aseptic meningitis [1]. We report the exceptional observation of a patient treated with Nivolumab for a melanoma who developed amyotrophic lateral sclerosis.

Case Presentation

A 58-year-old intellectually impaired patient, under curatorship, started an adjuvant treatment with Nivolumab for a melanoma IIIc (T4bN1bM0 8th AJCC).

Three Months (M3) after the beginning of the treatment, a dysphagia appeared. It was investigated by an otorhinolaryngology (ENT) examination and pharyngoesophageal transit that showed no abnormalities. Eso-gastro-duodenal fibroscopy showed chronic gastritis and subacute esophagitis.

At M6, swallowing disorders occurred, with persistence of dysphagia, and elevation of Creatine Phosphokinases (CPK). The hypothesis of dermatomyositis was evoked, a moderate improvement was noted under general corticotherapy 20 mg per day and decrease of CPK. The Dot myositis test was negative.

At M8, Nivolumab was stopped due to a loss of 6 kg and persistent dysphagia to both solids and liquids. A manometry was performed showing a non-specific tendency to hypocontractility on certain swallowing sequences.

At M12, due to the worsening of the dysarthria in parallel with the dysphagia, a brain Magnetic Resonance Imaging (MRI) was carried out and eliminated the presence of cerebral metastases. A

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new ENT consultation was performed and showed a quasi-immobile tongue, with the presence of numerous fasciculations, orienting towards an Amyotrophic Lateral Sclerosis (ALS).

Further investigations (Electromyogram (EMG)) could not be performed because the patient died 48 h later.

Discussion

We report the occurrence of a neurological syndrome suggestive of bulbar ALS that developed abruptly under ICI. The arguments in favor of this diagnosis are the disorders of phonation and swallowing, a quasi-immobile tongue, with the presence of numerous fasciculations reported at the ENT clinical examination. Complementary examinations could not be performed in our patient, who died just after the ENT consultation. The intellectual disability in our patient was a decoy, because the patient already had speech disorders.

The responsibility of iCI is debatable. In the literature, ALS has only been reported once as an adverse effect of ICIs: One case of ALS developed under Ipilimumab and Nivolumab [2]. This is a 63-year-old man with stage IV metastatic melanoma treated with ipilimumab and nivolumab. He had bradykinesia, shuffling gait and muscle cramps for 3 years. After one dose, the patient began to have generalized weakness which gradually worsened. The patient developed diplopia, lingual and upper/lower extremity fasciculations, and quick reflexes. The EMG revealed axonal neuropathy and diffuse denervation/reinnervation changes. Furthermore, an MRI displayed fatty replacement of the tongue with a bright tongue sign. These results pointed to the diagnosis of ALS superimposed onto myasthenic like syndrome. The patient died due to acute hypoxic respiratory failure.

Some authors have hypothesized an immune dysregulation in the pathogenesis of ALS [3], according to 3 possibilities: Inflammation and immunity have a direct role in causing ALS, affect the progression of disease, or are not directly involved in the disease. In their review, they critically evaluate reports investigating inflammation and the immune system in ALS pathogenesis. The data provide tantalizing clues that immune system components may indeed play a role in ALS pathogenesis, but results suggesting a causative or significant role in disease remain limited.

Conclusion

Despite the few cases described, it is important to think of ALS when phonation and swallowing disorders appear under immunotherapy.

References

1. Dalakas MC. Neurological complications of immune checkpoint inhibitors: What happens when you 'take the brakes off' the immune system. Ther Adv Neurol Disord. 2018;11:1756286418799864.
2. Jaffer M, Chung M, Sharda E, Ramsakal A, Peguero E, Verma N, et al. Immunotherapy induced myasthenic-like syndrome in a metastatic melanoma patient with amyotrophic lateral sclerosis. Clin Med Insights Oncol. 2020;14:1179554920978024.
3. Lyon MS, Wosiski-Kuhn M, Gillespie R, Caress J, Milligan C. Inflammation, immunity, and amyotrophic lateral sclerosis: I. Etiology and pathology. Muscle Nerve. 2019;59(1):10-22.