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Case Report: Malignant Melanoma treated with Ipilimumab and Nivolumab in Patient with Multiple Sclerosis

Tahir Abbas
Saskatoon Cancer Centre, Saskatchewan, Canada

Vinita Sundaram
Saskatoon Cancer Centre, Saskatchewan, Canada

ABSTRACT

This case report presents a patient with relapsing and remitting multiple sclerosis (MS) and metastatic malignant melanoma treated with combination immunotherapy. Ipilimumab and nivolumab was tolerated with no significant adverse events. There was no progression of multiple sclerosis while she received immunotherapy. This demonstrates that Ipilimumab and nivolimumab can be considered in patients with multiple sclerosis who require treatment with checkpoint inhibitors with close multidisciplinary monitoring.

Keywords: malignant melanoma, multiple sclerosis, immunotherapy, checkpoint inhibitors, ipilimumab, nivolumab.

INTRODUCTION

Immune check point inhibitors (ICI) have revolutionized the management of malignancies. Combination immunotherapy for malignant melanoma with ipilimumab (anti CTLA 4) and nivolumab (anti PD-1) revealed longer treatment free survival for combination therapy with unfortunately an increase in grade 3-4 adverse events [1,2]. While the ICI enhances the action of the immune system by blocking negative regulators of T cells, they also disrupt the immune homeostasis. The concern of life-threatening exacerbations of pre-existing autoimmune disorders due to ICI therapy excluded these patients in previous clinical trials [3]. Immune related adverse events (irAEs) are common with ICIs and include fatigue, rash, pruritis, diarrhea and nausea. Rare irAEs which are potentially more critical include neurological conditions such as Guilain Barre syndrome, encephalitis and myasthenia gravis.

The decision to provide immunotherapy to patients with pre-existing autoimmune disorders with the possibility of flares in neuroinflammatory activity triggering relapses requires a complex discussion due to evolving understanding of the long-term outcomes. Increasing number of patients with autoimmune disorders require immunotherapy, resulting in its cautious use with consideration of the risks and benefits. Fortunately, there is early identification and management of irAEs improving the safety of ICI therapy.

CASE PRESENTATION

In this case report we present a lady of 59 years with known multiple sclerosis since July 1987. She presented with optic neuritis of the right eye as clinically isolated syndrome, which failed to respond to steroids. Subsequently she had remitting and relapsing disease for which she

received pulse steroids. In March 2008, she was initiated on treatment with injections of Glatiramer acetate. Since then, she has had no further relapses. Her Expanded Disability Scale score was 5.

In September 2023 she underwent biopsy of right axillary node which was reported as cutaneous malignant melanoma of unknown primary (B Raf mutation negative). CT scan of brain, neck, chest and abdomen on 26 Sep 2023 revealed right axillary lymphadenopathy measuring 4.5 X 5.1 cm. No left axillary mediastinal or hilar lymphadenopathy was noted. Neither was a pleural or pericardial effusion noted or any aggressive bony lesions. She had a PET scan in October 2023 that showed intensely hypermetabolic right axillary lymph nodes with SUV of 24 measuring 5 X 4.5 cm. No other FDG avid disease was noted.

In view of unresectable stage 3 metastatic melanoma, she was offered treatment with Ipilimumab and Nivolumab. We had an in depth discussion on the benefits and risks of receiving combination ICI with pre-existing MS which may cause exacerbation of MS. She initiated therapy with Ipilimumab and nivolumab on November 23, 2023. When seen in the medical oncology clinic subsequently, she complained of a skin rash (grade 1). She responded to cortisone ointment and Benadryl tablets and was also provided with oral prednisone tablets. Her rash disappeared completely in 3-5 days. Her swelling in her right axilla was noted to have reduced in size. She had side effects of immune therapy such as fatigue and diarrhea. She complained of peripheral neuropathy (grade 1) of lower limbs which was treated by the MS clinic with gabapentin. Her ECOG status remained at 1 and she was able to carry out all her pre-disease activities without restriction. She completed the 4 cycles ipilimumab and nivolumab without any further adverse events and then was given maintenance protocol with single agent nivolumab for 4 cycles.

PET scan done in April 2024 revealed the right axillary node had decreased in size to 1.8cm with SUV 22. Reassessment by the surgeons considered this to be resectable and she underwent an axillary lymph node dissection in June 2024. Maintenance single agent nivolumab was given for a total of one year. Repeat CT scans at regular intervals showed no evidence of recurrence. She was followed up in the clinic and last MRI Brain on 24 Sep 2024 showed stable intracranial demyelinating disease. Her latest CT scan done in April 2025 reported no evidence of metastatic disease.

DISCUSSION

Combination therapy with ipilimumab and nivolumab significantly increases risk of immune related adverse events including neurological ones, when compared with monotherapy in those with autoimmune diseases [4]. There have been reports of severe neurological immune related adverse events and even exacerbation of MS in those patients treated with immune therapy [5]. The survival benefits of those with autoimmune disease were similar to non-autoimmune cohorts when treated with ICI [6]. This was found on retrospective analysis, but no multiple sclerosis specific efficacy data was available. At present there is no prospective data on the response of MS patients to ICI, and no information available about monotherapy versus combination ICI in this cohort.

We have observed in this case that combination ICI therapy is possible in MS patients when coupled with close multidisciplinary monitoring. A new trial (AIM-Nivo) by the National Cancer

Institute on the use of Nivolumab in patients with autoimmune disease and advanced, metastatic and unresectable cancer may eventually shed more light on this [7]. Canada has one of the highest prevalence rates for Multiple Sclerosis [8]. Within Canada, Saskatchewan has a higher prevalence than many other provinces. While ICIs have transformed melanoma treatment, their safety in patients with pre-existing autoimmune diseases, such as Multiple Sclerosis, remains unclear due to limited clinical data and the frequent exclusion of such patients from clinical trials [6,9]. MS is an immune-mediated disorder characterized by T-cell dysregulation, and multiple case reports have documented severe MS exacerbations following ICI therapy [1,2,5]. Retrospective cohort analyses indicate that patients with autoimmune diseases, including MS, experience higher rates of irAEs, particularly neurological toxicities, when treated with ICIs [3,6,10,12].

Glatiramer acetate (GA) is a common immunomodulatory therapy for MS that induces regulatory T-cell activity and skews immune responses toward an anti-inflammatory phenotype. However, no studies have directly examined the interaction between GA and ICIs in melanoma patients with MS, creating a significant knowledge gap. There has been no clinical evidence available regarding possible interactions between ICIs and Glatiramer. Existing research on neurological irAEs from ICIs suggests that demyelinating complications and central nervous system toxicity are rare but severe, particularly in oncology patients with pre-existing neuro-autoimmune conditions [12,13,15]. Case reports document new-onset demyelination, encephalitis, and exacerbation of MS symptoms following ICI initiation [5,12,14,15].

Given the increasing use of ICIs in melanoma treatment and the expanding population of patients with pre-existing autoimmune diseases, further prospective studies are critically needed to optimize treatment strategies and mitigate risks. Factors which may be considered are patients age, inactivity of MS disease and use of disease modifying therapies. While there is caution in the use of ICI therapy in MS it is not an absolute contraindication and must be assessed on a case-by-case basis.

CONCLUSION

There is a paradigm shift to provide patients with autoimmune disease with the benefit of treatment with immunotherapy. In previous clinical trials we excluded patients with autoimmune disease due to risk of exacerbation. We speculate that the risks are considerably reduced when the autoimmune disease is well controlled on treatment. A recent ongoing clinical trial will provide us with the necessary information to safely utilize the benefits of immunotherapy in patients with autoimmune disorders.

References

1. Wolchok JD, Chiarion-Sileni V, Gonzalez R, et al. Long-Term Outcomes with Nivolumab Plus Ipilimumab or Nivolumab Alone Versus Ipilimumab in Patients with Advanced Melanoma. J Clin Oncol. 2022;40(2):127-137. doi:10.1200/JCO.21.02229.

2. Hodi, F Stephen et al. Combined nivolumab and ipilimumab versus ipilimumab alone in patients with advanced melanoma: 2-year overall survival outcomes in a multicentre, randomised, controlled, phase 2 trial. The Lancet Oncology, Volume 17, Issue 11, 1558 – 1568. Doi: 10.1016/S1470-2045(16)30366-7.

3. Brown LJ, Weppler A, Bhave P, et al. Combination anti-PD1 and ipilimumab therapy in patients with advanced melanoma and pre-existing autoimmune disorders. J Immunother Cancer. 2021;9(5): e002121. doi:10.1136/jitc-2020-002121.

4. Reid P, Abdel-Wahab N. Safety and effectiveness of combination versus monotherapy with immune checkpoint inhibitors in patients with preexisting autoimmune diseases. Oncoimmunology. 2023;12(1):e2205861 .

5. Quinn CM, Kister I. Neurologic outcomes in people with multiple sclerosis treated with immune checkpoint inhibitors for oncologic indications. Neurology. 2024;103(11): e210003. doi:10.1212/WNL.0000000000210003.

6. van der Kooij MK, Kapiteijn E. Safety and efficacy of checkpoint inhibition in patients with melanoma and preexisting autoimmune disease. Ann Intern Med. 2021;174(5):641-648. DOI.10.7326/m20-3419

7. Dumbrava EE, Dougan ML, Gupta S, et al. A phase 1b study of nivolumab in patients with autoimmune disorders and advanced malignancies (AIM-NIVO). J Clin Oncol. 2021;39(15_suppl): TPS2676-TPS2676. doi: 10.1200/JCO.2021.39.15 suppl. TPS2676

8. Public Health Agency of Canada, "Multiple sclerosis in Canada," Canada.ca, May 29, 2024. https://www.canada.ca/en/public-health/services/publications/diseases-conditions/ multiple-sclerosis-infographic.html.

9. Menzies AM, Long GV. Anti-PD-1 therapy in patients with advanced melanoma and preexisting autoimmune disorders or major toxicity with ipilimumab. Ann Oncol. 2016;27(4):724-730.

10. Das N, Reddy D. Adverse neurologic complications following immune checkpoint inhibitors for treatment of melanoma: Comparative analysis of PD-1 inhibitor monotherapy to combination therapy with CTLA-4 inhibitors. Neuro-Oncol. 2024;26(8-suppl)218. doi.10.1093/neuonc/noae165.0860

11. Schmidt T, Glas M. Pseudomeningeosis and demyelinating metastasis-like lesions from checkpoint inhibitor therapy in malignant melanoma. Front Oncol.2021; 11:754253. doi; 10.3389/fonc.2021.637185

12. Mancone S, Strowd R. Neurological complications of immune checkpoint inhibitors: a case series (P4.159).J Neurol. 2018;265(7):1636-1642. Doi:10.1007/800415-081-8890-z

13. Yan C, McGinley MP. Predictors for the development of neurological immune-related adverse events of immune checkpoint inhibitors and impact on mortality. EurJNeurol.2023;30(10):3321-3327. Doi.10.1111/ene.15942.

14. Vaddepally R, Kumar N. Case Report: A case of immune checkpoint inhibitor therapy in a patient with multiple sclerosis. F1000Research. 2020; 9:954.

15. Garcia CR, Jayswal R, Adams V et al. Multiple sclerosis outcomes after cancer immunotherapy. Clin Transl oncol. 2019;21910):1336-1342. Doi:10.1007/s12094-019-02060-8.