

## Bilateral Uveitis Following Nivolumab Therapy for Metastatic Melanoma

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Received: January 08, 2020; Published: February 27, 2021

### Abstract

**Background:** We report a case of a 54 years old female presenting with bilateral uveitis associated with Nivolumab infusions for metastatic melanoma. The patient underwent successful treatment of both eyes with ophthalmic topical medications.

Uveitis has been reported as a side effect of Nivolumab treatment.

**Conclusion:** Physicians should be aware of the possible ocular inflammatory complications following the use of Nivolumab and provide the best treatment.

**Keywords:** Nivolumab; Uveitis; Melanoma; Immunotherapy; Side-Effect; Programmed Cell Death-Protein 1

### Abbreviations

anti-PD-1: Anti-Programmed Cell Death Protein-1; FDA: Food and Drug Administration; OCT: Optical Coherence Tomography; OD: Oculus Dexter; OS: Oculus Sinister; OU: Oculus Uterque; CTLA-4: Cytotoxic T-Lymphocyte-Associated Protein 4; irAEs: Immune-Related Adverse Events

### Introduction

Nivolumab is an anti-programmed cell death protein-1 (anti-PD-1) monoclonal antibody, a class of immune checkpoint inhibitors [7]. It has been approved by the Food and Drug Administration (FDA) mainly for metastatic melanomas as well as other tumours like metastatic non-small cell lung cancer, Advanced renal cell carcinoma, classical Hodgkin's lymphoma and squamous cell carcinoma of the head and neck and is routinely used in clinical practice [3]. Generally, the side effects are immune related adverse events like colitis, pneumonitis, tubulointerstitial nephritis and hepatitis [7].

We report a case of bilateral uveitis secondary to Nivolumab infusions for metastatic melanoma.

### Case Presentation

A 54 years old female presented with bilateral blurred vision associated with floaters and photophobia of 3 months duration. Patient is diagnosed with recurrent metastatic melanoma with metastasis to brain, left adrenal gland, right ovary, left axillary lymph node and lung metastases. The primary melanoma located on the Scapula had been removed seventeen years earlier. Patient was started on a single agent Nivolumab 480 mg q4 weekly 7 months before her first visit to the ophthalmology clinic.

Past medical history revealed that the patient was diagnosed with right Breast CA, ER-ve/PR -ve, HER2 positive, in 2008 wherein patient underwent chemotherapy (5 fluorouracil, Epirubicin, Cyclophosphamide followed by Taxotere (Herceptin) and right mastectomy and axillary lymph node dissection and adjuvant radiotherapy. Recent mammogram showed left axillary mass lesions suggestive of metastatic lymphadenopathy, with no suspicious lesion in breast. Axillary mass biopsy revealed malignant melanoma. Recent CT abdomen and pelvis, and brain MRI both showed a good response to Nivolumab, manifested by the decrease in size, number, degree of enhancement of the brain metastasis previously seen.

Ophthalmologic evaluation showed visual acuity of 6/6.67 OD, 6/8.3 OS. Intraocular pressure (IOP) via Non-contact tonometry was 14 mm Hg OU. Slit lamp examination in both eyes indicated the presence of +2 anterior chamber cells and flare, and posterior synechiae and keratic precipitates. Dilated fundus examination showed presence of + vitreous cells, an attached retina with flat macula. No retinal or choroidal lesions seen, no vasculitis. Patient was given Prednisolone 1% eye drops QID and Cyclopentolate 1% BID OU. After two months of topical steroid tapering dose, vision improved to (6/6 OD, 6/6.7 OS) and with no inflammation.

### Discussion

Nivolumab is a fully human immunoglobulin G4 PD-1 immune checkpoint inhibitor antibody used clinically in the treatment of metastatic melanomas. Works by blocking the PD-1 signalling pathway, so it can restore the patient's T-cell mediated anti-tumor immunity [7]. This alters patient's immune tolerance and causes 'immune-related adverse events' (irAEs), which presents as autoimmune-like inflammatory disease. For Nivolumab, the most common irAEs seen in Phase I-III clinical trials were fatigue, rash, pulmonary disease and endocrinopathies [6].

Skin melanocytes share many surface proteins as the human uvea tissues and retina, both contain melanocytes, and melanin pigment. To treat melanoma, immune checkpoint blockade is used to enhance immune reactions, it triggers the autoantibodies against normal melanocytes in uvea as well, leading to uveitis [4].

To our best knowledge, PD-1+ T-cells have been shown to be involved in uveitis [5], as it acts directly on the PD-1 receptors, so it is possible that Nivolumab is the aetiology of our patient's uveitis.

Uveitis emerged as an irAE in some patients received Nivolumab and all responded to topical or intraocular steroids [1,2,8,9].

### Conclusion

It is crucial to increase awareness among oncologists of uveitis as a side effect of Nivolumab. Ophthalmologist should be involved in multidisciplinary team, the team should coordinate to provide the best care to diagnose and manage the primary pathology and to manage the side effect of the treatment as well. ophthalmologic manifestations are quickly recognized and can be adequately managed.

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**Volume 12 Issue 3 March 2021**

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