Letter to the Editor

**Bilateral ipilimumab-induced posterior uveitis following
treatment for metastatic choroidal melanoma**

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Ipilimumab is a CTLA-4 monoclonal antibody that amplifies T-cell activation and response to melanoma. It is approved to treat unresectable or metastatic melanoma. Immune-related adverse events are common (up to 90% of patients), and include colitis, hypophysitis, hypothyroidism, hepatitis and dermatitis.¹ 1.3% of patients suffer from ocular side effects, such as scleritis, anterior uveitis and Grave's-type ophthalmopathy.² This report presents a novel case of bilateral posterior uveitis in a patient receiving ipilimumab for metastatic choroidal melanoma and summarises the literature regarding treatment options for patients with ocular immune-related adverse events.

A 27-year-old female presented with a choroidal melanoma in her right eye, which was treated with a 20mm Ruthenium plaque. There was complete regression of the tumour, but she subsequently developed cystoid macular oedema as a result of radiation retinopathy. This responded to intravitreal aflibercept and her acuity returned to 6/5.

She developed systemic metastatic disease 3 years following brachytherapy and was treated with ipilimumab. She then presented with decreased vision of 6/9.5 in each eye after the third dose. The anterior chamber was quiet and there were no cells or haze in the vitreous. Fundus examination revealed bilateral pale chorioretinal lesions, which on optical coherence tomography appeared as atypical intraretinal cysts in addition to extensive architectural changes in the retina from the outer plexiform layer to the ellipsoid zone (Figure 1).

Figure 1: A) Optos colour image of the right macula, showing scars from previous treatment. B) Optos colour image of the left macula. Optical coherence tomography scans through the C) right, and D) left macula.

Fluorescein angiogram showed cystoid macular oedema and foci of leakage consistent with choroiditis, in addition to vascular leakage in the inferior retina secondary to radiation retinopathy from the previous brachytherapy (Figure 2).

Figure 2: Wide-field fluorescein angiography of the right and left eyes.

The patient concurrently developed a skin reaction and an autoimmune hepatitis while the uveitis was still active. In consultation with the patient's oncologist, the decision was made to not pursue further cycles. A short course of intravenous methylprednisolone therapy was instituted, followed by oral prednisolone, which resulted in resolution of ocular inflammation over 6 weeks and a return of vision to 6/4.8 bilaterally. Unfortunately, the patient passed away shortly thereafter due to progressive metastatic omental disease.

Ipilimumab can trigger a systemic autoimmune response, with only 1-2% of patients developing ocular side effects, which include episcleritis, conjunctivitis, anterior uveitis, Vogt-Koyanagi-Harada-like syndrome, optic neuritis and a thyroid-like orbitopathy.³ These are typically treated with systemic corticosteroids and withdrawal of therapy. Refractory cases may require additional immunosuppression, including intravenous immunoglobulin, infliximab and plasmapheresis.¹

We report here a patient who developed multiple immune-related adverse events, including posterior uveitis and hepatitis. To our knowledge this is the first reported case of bilateral choroiditis with cystoid macular oedema and outer retinal cavitation from ipilimumab therapy for metastatic choroidal melanoma. A previous case report has described bilateral choroidopathy and serous retinal detachments after 4 cycles of ipilimumab for cutaneous melanoma.⁴ Choroidal findings in ipilimumab-related

uveitis may share the same pathophysiology as ipilimumab-related vasculopathies reported elsewhere in the body.⁵

This case, along with the current literature, suggests that the onset of severe ocular inflammation may necessitate discontinuation of ipilimumab and treatment with systemic corticosteroids for preservation of visual function.

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