Reversible BRAF inhibitor-induced acute exudative paraneoplastic polymorphous vitelliform maculopathy

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A 72-year-old Caucasian male was receiving vemurafenib and pembrolizumab treatment for BRAF VK600K mutation-positive metastatic cutaneous melanoma. He was initially started on vemurafenib alone, with pembrolizumab being added to therapy 3.5 months later.

He developed bilateral central scotomas six weeks after starting vemurafenib but prior to commencing pembrolizumab. He was reviewed by the ophthalmology service 3.7 months after commencing vemurafenib and one week after commencing pembrolizumab. Presenting vision was 6/9 right eye and 6/12 left eye.

Examination revealed bilateral blunted foveal reflexes (Figure 1). Fundus autofluorescence showed some hyper-autofluorescence centrally (Figure 2), and optical coherence tomography revealed bilateral neurosensory detachments (Figure 3). A diagnosis of acute exudative paraneoplastic polymorphous vitelliform maculopathy (AEPVM) secondary to vemurafenib (BRAF inhibitor) was made. Vemurafenib was discontinued and lesions resolved with vision improving to 6/6 in both eyes (Figure 4) within eight weeks of stopping vemurafenib. Pembrolizumab was continued without ocular complications, but the cancer progressed with new cerebral metastases.

Due to progressive metastatic disease, he was restarted on vemurafenib four months after the drug was initially discontinued but developed recurrence of AEPVM within two weeks of restarting vemurafenib.

Complete resolution of AEPVM following discontinuation of vemurafenib with recurrence on re-exposure to the drug suggested a causal relationship between vemurafenib and AEPVM.

Newer immune cancer therapies provide targeted therapy that increases survival for those with metastatic disease. Ocular complications associated with BRAF inhibitors typically include uveitis; AEPVM is rare. Aetiologic possibilities include immune-mediated inflammation, drug toxicity and idiosyncratic reaction.

Increased knowledge of the adverse ocular effects associated with these medications is necessary, and patients should be counselled to report visual symptoms on commencing these therapies. Prompt review of visual complaints is necessary to exclude uveitis and AEPVM.

These medications are lifesaving. Treatment is complex and requires careful discussion with the treating oncologists. Options may include local corticosteroids, switching immune therapy agents and medication cessation, but with risk of disease progression.
**Figure 1:** Widefield colour fundus photographs of right and left eye with blunted foveal reflexes.

**Figure 2:** Short-wavelength fundus autofluorescence showed a slight increase in autofluorescence centrally.
Figure 3: Heidelberg HRA Spectralis OCT scans (Heidelberg Engineering, Heidelberg, Germany) of right and left eye at presentation showing bilateral neurosensory retinal detachments.

Figure 4: Heidelberg HRA Spectralis OCT scans (Heidelberg Engineering, Heidelberg, Germany) of right and left eye at presentation showing resolution of bilateral neurosensory retinal detachments following discontinuation of vemurafenib.
Competing interests:
Nil.

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