

Vogt-Koyanagi-Harada disease-like posterior uveitis in the course of Dabrafenib-Trametinib for adjuvant melanoma treatment

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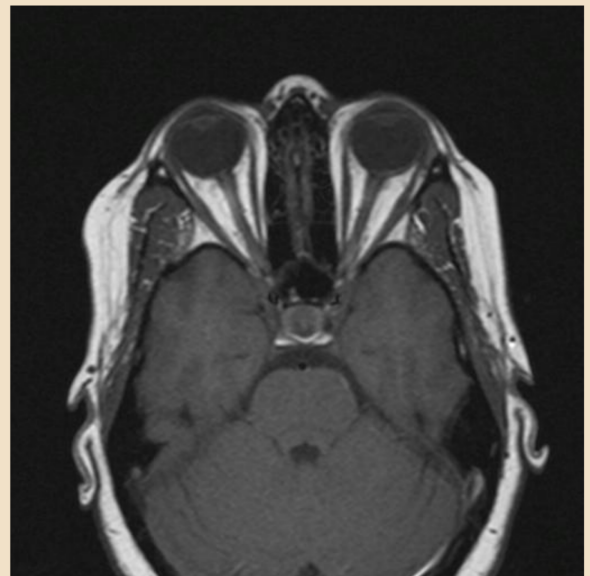
Introducción and Objectives: Although uveitis is reported as an uncommon adverse event (AE) associated with dabrafenib and trametinib, the occurrence of severe uveitis is extremely rare. We describe a case of Vogt-Koyanagi-Harada (VKH)-like uveitis developing after the administration of dabrafenib/trametinib adjuvant therapy in a young patient with stage III melanoma.

Material and methods: case report and review of literature

Case report: Female patient, 37 years old, Fitzpatrick phototype II that was diagnosed on October 2018 with a right ulcerated scapular melanoma Breslow 1,6mm. SLNB of the right axillary region showed a metastatic melanoma in two nodes. Axillary lymph node dissection detected metastases in 5/22 nodes. PET/CT scan showed no evidence of distant metastatic disease. Molecular testing detected a BRAF V600E mutation starting an adjuvant treatment with dabrafenib 150 mg orally twice daily and trametinib 2 mg orally once daily.

Six months after commencing the targeted therapy, she presented with 2 days of blurred vision, decreased of visual acuity in the left eye, with no associated eye pain, headache, redness, or floaters as well as negative viral serology. In the ocular exam, it was seen a slightly edema in the retina suggesting CFN (cellular fibronectin).

MRI, Optical coherence tomography (OCT) and B-scan mode ultrasonography confirmed a serous retinal detachment. Ophthalmologist diagnosed Vogt-Koyanagi-Harada disease-like posterior uveitis. The patient was treated with a bolus of methylprednisolone, and then oral dexamethasone. Although suspending dabrafenib/trametinib treatment, the patient could not recover yet the visual acuity lost in her left eye.



Conclusion: The most common ocular side effect with BRAF inhibitors is uveitis (1% of patients treated with dabrafenib in clinic trials and 2.1% of patients with vemurafenib). In a systematic review of ocular toxicity trametinib was associated with central serous retinopathy in 1.5–2% of cases, with retinal venous occlusion in 0.5% of cases and blurred vision in 4% of cases. Vogt-Koyanagi-Harada (VKH) disease is a rare multi-system auto-inflammatory disease with bilateral granulomatous panuveitis with serous retinal detachment as described in our patient. It can be associated with other neurologic symptoms. Its pathogenesis is likely multifactorial, and has been incompletely elucidated. T-cell mediated inflammation may cause selective damage to melanocytes, leading to acute visual blurring and retinal detachment. The exact cause of VKH-like ocular signs during BRAF-MEK therapy is not yet entirely explained. There are few cases, reported in the literature and all of them associated with metastatic melanoma. Although it is not clear if the treatment should be definitely suspended, in this case it was on adjuvant intention and thus we decided to suspend it.



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