Ocular inflammation - Panuveitis during Anaplastic Thyroid Cancer treatment with dabrafenib and trametinib

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Background

- The Anaplastic Thyroid Cancer (ATC)[1] is a rare (<2% of all thyroid gland neoplasms), highly aggressive malignant tumour, often metastatic.
- The molecular pathogenesis of ATC includes mutations in the Ras-Raf-MEK-ERK pathway.
- Combined therapy with Dabrafenib (BRAFi) and Trametinib (MEK1/2i) had been approved for the treatment of unresectable or metastatic ATC with the BRAF V600E mutation, *BRAF*V600 mutation–positive skin cutaneous melanoma (SCM)[2] and non-small cell lung cancer (NSCLC)[3].

Case

- Male Caucasian 58 years old with ATC Stage IV under chemotherapy with Dabrafenib and Trametinib presented with reduced vision bilaterally.
- The Visual acuity (VA) was OD 20/70 and OS 20/50. Slit lamp examination revealed no pathological findings. Fundoscopy showed a bilateral Central Serous Chorioretinopathy (CSRCR) with intact optic discs.
- Optical Coherence Tomography (OCT) identified subretinal fluid (SRF) in the left eye and peripheral neurosensory retinal detachment (RD) in both eyes (Figure 1).
- The patient was treated with topical corticosteroids and discontinuation of the chemotherapy.
- After complete recovery, the patient was treated with dabrafenib monotherapy. After the addition of trametinib, the patient presented with foreign body sensation and eye redness in both eyes.
- VA was intact. Examination showed iridocyclitis with anterior chamber cells, progressive development of aqueous flare, posterior synechiae and circumlimbal injection. Single therapy with dabrafenib was followed along with topical cyclopentolate and dexamethasone.
- The patient progressively developed a flare of iridocyclitis with posterior synechiae bilaterally, left cystoid macular oedema and unilateral VA reduction.
- Chemotherapy was completely stopped (Figure 2) and oral corticosteroids were added.

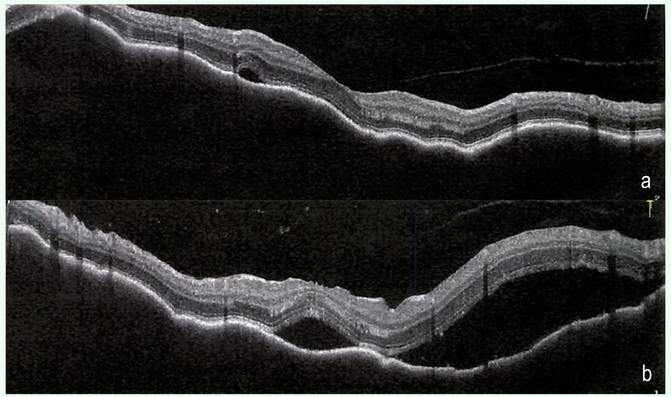


Figure 1: OCT RE (a) and LE (b) at first examination under dabrafenib and trametinib

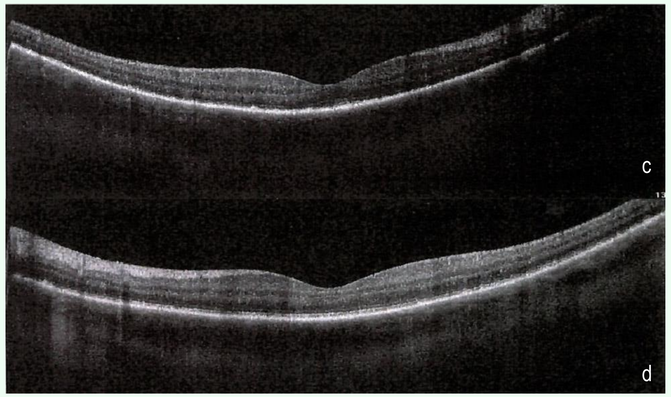


Figure 2. OCT RE (c) and LE (d) after chemotherapy discontinuation

Conclusion

- Corticosteroids and discontinuation of the chemotherapy led to the resolution of the inflammation.
- Although there have been reports of ocular side effects with this class of drugs in BRAFV600 mutation positive SCM and NSCLC, uveitis in ATC under monotherapy with dabrafenib has not been previously reported.
- Strict ophthalmological follow up and imaging review is recommended in patients with ATC under chemotherapy with Dabrafenib with or without Trametinib
- Further investigation should be conducted to identify factors that may prioritise certain patients at higher risk for this complication.

References

1. US Food & Drug Administration, FDA approves new uses for two drugs administered together for the treatment of BRAF-positive anaplastic thyroid cancer, May 04, 2018

2. Sharny et al., Ocular Toxicity due to Trametinib and Dabrafenib, BMC -- Ophthalmol. 2017 Aug 17;17(1):146.doi: 10.1186/s12886-017-0541-0.

3. Chalmers et al., Adverse Event Management in Patients with BRAF V600E-Mutant Non-Small Cell Lung Cancer Treated with Dabrafenib plus Trametinib, Oncologist. 2019 Jul;24(7):963-972.doi: 10.1634/theoncologist.2018-0296.Epub 2018 Dec 31.22