Edema and separation of outer retinal layers secondary to selumetinib

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INTRODUCTION

- MEK inhibitors are new therapeutic agents targeting the MAP-Kinase pathway and are currently being evaluated in phase 1 & 2 clinical trials for pediatric brain tumors.

- Ophthalmologic side effects have previously only been reported in adults and include:
  - Retinal vein occlusion, central retinal artery occlusion and separation of the neurosensory retina.

- We present 2 patients with optic pathway gliomas who developed outer-retinal layer separation visualized by SD-OCT while taking the MEK inhibitor selumetinib.

METHODS

- Each patient underwent SD OCT as part of a clinical visit (Case 1) or research visit (Case 2).

- **Case 1:** 13 y/o female patient complaining of two days of “large raindrops” obscuring her central vision
  - Spectralis: 9.2mm x 7.6mm, 61 line volume
  - Case 2: 6 y/o, autistic, non-verbal male patient
  - Bioptigen: 6mm x 6mm, 300 x 300 volume

- Each patient had multiple previous visits for comparison

CASE 1

A. Pre-event

B. Event

- Six months after starting selumetinib, patient presented complaining of two days of continuous visual phenomenon described as “large rain drops” that would obscure her central vision in both eyes. Exam was unremarkable with a stable visual field defect. Macular SD-OCT scans visualized separation and a new highly reflective band between the retinal pigmented epithelium (RPE) and the ellipsoid segment (arrow). Infrared (IR) images showed questionable signal changes around the fovea (*). Selumetinib was stopped.

D. Within 2 days of stopping selumetinib, her visual symptoms resolved. Repeat examination, 12 days after stopping selumetinib, demonstrated the OCT findings had resolved.

CASE 2

A. Macular SD-OCT acquired during sedation was qualitatively normal prior to starting selumetinib.

B. Seven months after starting selumetinib, his OCT demonstrated separation across the RPE and interdigitation zone.

C. After holding selumetinib for 7 days, repeat OCT demonstrated complete resolution of the macular findings.

D. Patient was restarted on selumetinib at the same dose and OCT imaging 6 weeks, 3 months and 6 months (left) later demonstrated continued resolution of the macular findings.

E. 8 months after restarting selumetinib, the retinal separation returned.

DISCUSSION

- Retinal separation occurred approximately 6 months after initiating selumetinib in both patients.

- We suspect that our patients did not experience any long term side effects from their retinal changes.

- We can only speculate how these RPE changes would evolve if treatment continued and whether they would result in the previously reported side effects such as retinal vein occlusion, retinal detachment, or permanent RPE abnormalities.

- Clinicians caring for children on MEK inhibitors, especially those with visual pathway tumors, should be aware of the potential retinal side effects and consider SD-OCT imaging as part of their ophthalmologic evaluation, especially in pre-verbal or uncooperative children, or those complaining of unusual visual phenomenon.

Separation of outer retinal layers secondary to selumetinib.

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