A CASE OF DRUG-INDUCED CYSTOID MACULAR EDEMA ASSOCIATED WITH THE TREATMENT OF MS

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INTRODUCTION

Fingolimod, the first FDA-approved oral agent for the management of relapsing forms of multiple sclerosis (MS), hinders the trafficking of lymphocytes involved in the immune-mediated process of MS. Phosphorylation of fingolimod results in fingolimod-phosphate, which shares structural similarities with sphingosine-1-phosphate (S1P) in vivo. [3] The S1P receptors are found on lymphocytes and other organs. Reducing lymphocyte upregulation and their migration from lymphoid tissue to the circulation has the desired therapeutic effect in MS, protecting the central nervous system from attack by myeline-reactive lymphocytes. [2,3] The destruction of S1P receptors in other organs is responsible for several complications, such as nasopharyngitis, cardiovascular complications (bradycardia, hypertension, heart block) and ocular side effects. Fingolimod-associated macular edema (FAME) is the most common ocular side effect but retinal hemorrhages and retinal vein occlusion can occur. [3] Fingolimod phosphate (PP) has shown to have secondary effects on vascular endothelial barrier function, thereby potentially compromising the blood-retinal barrier. [2]

CASE PRESENTATION

A 68-year-old female patient presented with symptoms of bilateral blurred vision and acute pain in the left eye. Her past medical history included multiple sclerosis (MS), emotional disturbance, dyslipidemia, arterial hypertension but no history of diabetes mellitus. She was on fingolimod 0,5mg/day treatment for 8 years and she is smoking for 50 years. Additionally, two years ago, she underwent cataract surgery in both eyes.

During the physical examination her best corrected visual acuity (BCVA) was 4/10 in the right eye and 3/10 in the left eye, her intraocular pressure in both eyes was 11mmHg, she had mild color disturbance and relative afferent pupillary defect (RAPD) was negative. Funduscopic examination revealed bilateral dull foveal reflex (figure 3). Optical Coherence tomography (OCT) scan demonstrated intraretinal fluid, foveal cyst and increased central macular thickness (figure 1). Brain MRI exam remained stable and the orbital MRI was clear.

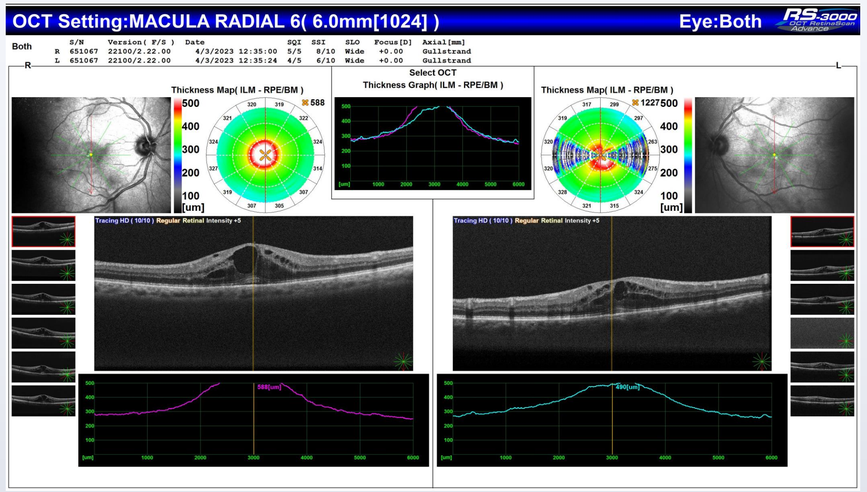

Figure 1. OCT-Cystoid macular edema

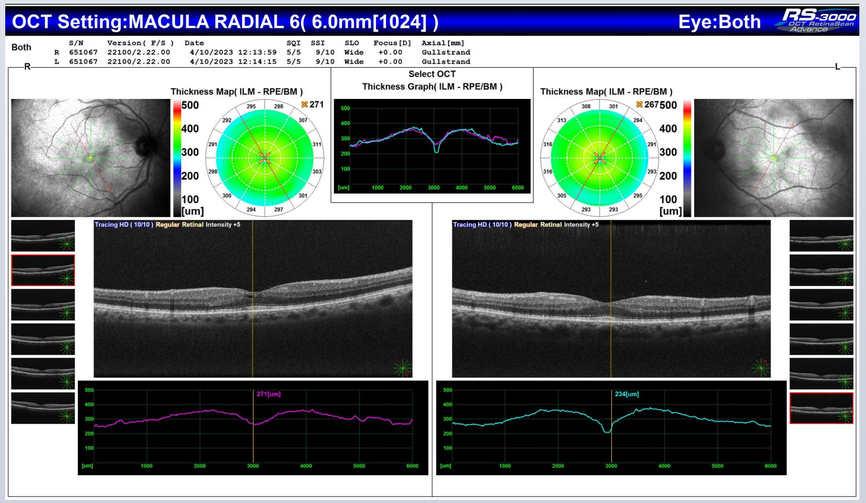

Figure 2. OCT 7th day under treatment for ME.

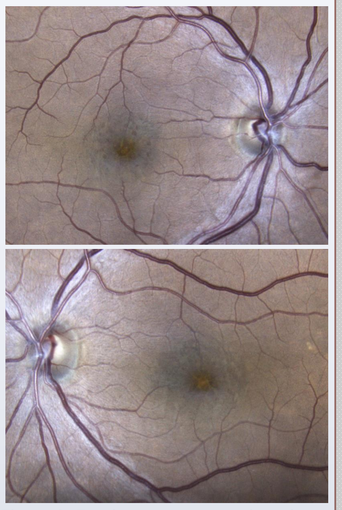

Figure 3. Fundus camera-macular edema.

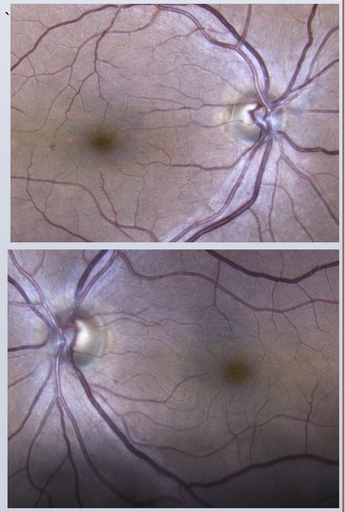

Figure 4. Fundus camera-macular edema subsided.

MANAGEMENT

Treatment was initiated with oral acetazolamide, and steroid and NSAIDs drops. The drug suspected- fingolimod was discontinued arbitrarily by the patient within 3 days, without her Neurologist's consultation. The macular edema subsided within 7 days (Figure 2,4) and BCVA was 8/10 in her right eye and 10/10 in her left eye. There has been no recurrence of macular edema (ME) and her Neurologist hasn't restarted the treatment, but the question arises whether she can continue fingolimod therapy.

DISCUSSION

FAME-related case reports were included in pooled analysis by searching databases from 2010 since 2022.[2] According to this there are a number of ocular conditions that have been linked to FAME, the only ocular condition that has been mentioned in the FREEDOMS and TRANSFORMS studies. [3]

According to this studies, the fingolimode effects on the eye is often asymptomatic may be the reason for the stipulation by NICE for routine ophthalmic screening with OCT and visual acuity (VA) at 3-4 months in all patients commencing fingolimode therapy. [1,3,2]. A screening protocol based on the patient's medical history, OCT results, and VA was suggested by NICE guidelines.[3] Higher risk patients of FAME associated with history of uveitis, diabetes, prior cataract surgery and fingolimode dose-dependence. [1,4]

CONCLUSION

Previous studies have established the risk factors of FAME and the guidelines for screening of patients treated with fingolimod which includes ophthalmic examination and taking a detailed medical history. Despite this, there is no established therapeutic protocol for the management of FAME yet, which largely depends on the severity and individual health condition. In some cases discontinuing the medication may be necessary, while in others, managing the ME itself might be more appropriate. The treatment decision is typically made by the collaboration between Neurologists and Ophthalmologists based on the patient's overall health, the severity of ME and the underlying condition being treated with fingolimode.

References

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