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SHORT COMMENTARY

Does fingolimod in multiple sclerosis patients cause macular edema?

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Abstract Multiple sclerosis (MS) is a demyelinating disease of the central nervous system and is the common cause of optic neuritis. Fingolimod, an immunosuppressive agent, is used in MS to prevent acute exacerbations. We report a case of relapsing–remitting MS treated with fingolimod. The patient presented with an acute decrease in vision in the left eye. Eye examination showed clinical macular edema (ME) in the left eye, which was confirmed on fluorescein angiogram and optical coherence tomography (OCT). After discontinuation of fingolimod and treatment with topical corticosteroid medication, there was complete resolution of the ME. The ME as a side-effect of fingolimod is reversible after discontinuing, which was seen on OCT.

Keywords Fingolimod · Multiple sclerosis · Macular edema

Introduction

Multiple sclerosis (MS) is a demyelinating disorder of the central nervous system (CNS). It is associated with waxing and waning of symptoms producing a "relapsing–remitting (RR)" clinical presentation. The therapeutic modalities to MS include interferon-β, monoclonal antibodies such as rituximab, ocrelizumab, and ofatumumab [1]. FTY720/fingolimod (commercial name Gilenya; Novartis) a novel medicine, is the first oral MS therapeutic agent found to be useful for RRMS [2–6]. The common adverse effects reported with fingolimod were influenza, headache, diarrhea, liver enzyme elevation, bradycardia, herpetic infections, and respiratory illness [5–7]. Few studies have reported the association of macular edema (ME) as a side-effect of fingolimod [5–7]. We report the ophthalmological and image-guided (optical coherence tomography–OCT) findings showing clinical resolution of ME in MS patient following discontinuation of fingolimod and attributes the cause of ME to fingolimod, and we feel our case will be an addition to the current literature.

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Case description

A 52-year-old man noted sudden blurring of vision in the left eye (OS). He had a past history of MS for 8 years. He developed optic neuritis in the right eye (OD) few years ago. He was started on fingolimod (0.5 mg) 3 months ago for the treatment of RRMS. There was central distortion of lines on the Amsler grid. Visual acuity was 20/20 in both eyes. Anterior segment examination of both eyes was unremarkable. Fundus examination OS revealed clinical cystoid macular edema (Fig. 1a) without evidence of hemorrhages, drusen, or exudates. Fundus examination OD showed mild optic disc pallor, no clinical ME or hemorrhages, and normal retina periphery (Fig. 1b). Fluorescein angiogram and Indocyanine Green angiogram on the OS showed diffuse parafoveal leakage in the late phases secondary to the macular edema (Fig. 1c), whereas there was no leakage in the OD (Fig. 1d). OCT (Cirrus^{TM} High-Definition Spectral Domain Technology, Zeiss) showed distortion of the foveal contour with cystoid macular edema in the OS (Fig. 2a). The central foveal thickness on OCT in OD was 280 μm and in OS was 502 μm. The etiology for ME in the left eye was considered as a side-effect of fingolimod. Fingolimod was discontinued. ME

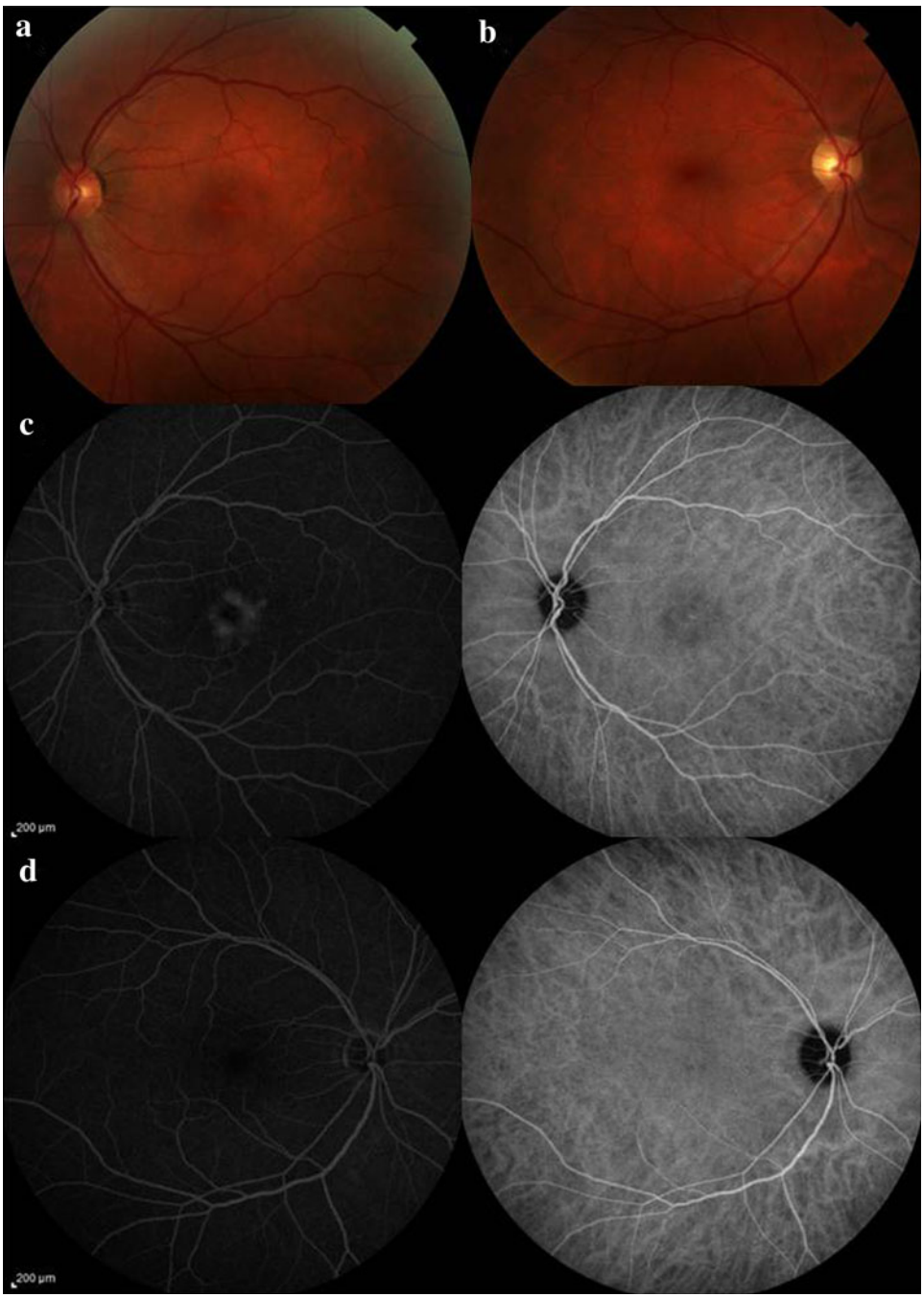

Fig. 1 Color fundus photograph of the left eye showing clinical macular edema (**a**) and right eye showing normal macula (**b**). Fluorescein angiogram/Indocyanine Green angiogram showing leakage in the macula of the left eye (**c**) and no leakage in right eye (**d**)

was treated with topical prednisolone acetate medication. At 3 months of follow-up, there was complete resolution of ME both clinically and on OCT (Fig. 2b). After discontinuing the fingolimod, OCT measured the central foveal thickness in OD as 276 µm and in OS as 303 µm.

Discussion

Fingolimod acts on the sphingosine-1 phosphate receptors and reduces the migration of lymphocytes into the CNS in RRMS [8]. ME as a side-effect of fingolimod was reported in renal transplant patient by Saab and associates [7]. The duration to develop ME after starting fingolimod was considered to be approximately 3 months in the clinical trials [9]. In the FREEDOMS trail ($n = 1{,}272$), ME was noted in 0.4% of the patients [9]. In a phase II study using oral fingolimod on 281 patients, at 36 months follow-up, only four patients were noted to have the clinical ME. When the central foveal thickness was measured by using the OCT, 70% of patients on fingolimod had values between −20 and +20 µm and with stable visual acuity in

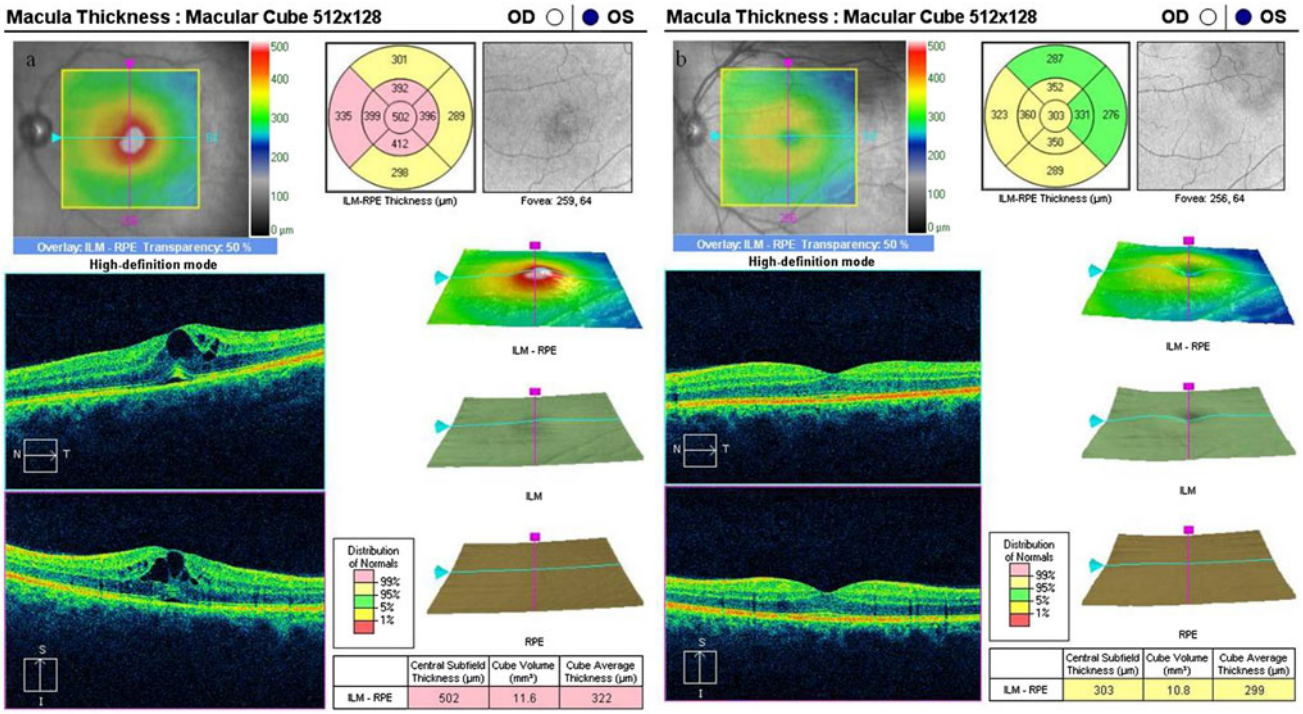

Fig. 2 Optical coherence tomography (Cirrus^{TM} High-Definition Spectral Domain Technology, Zeiss) showing cystoid macular edema in the left eye (**a**) with complete resolution of the macular edema after discontinuation of fingolimod (**b**)

all patients [3]. Our study patient also developed ME in 3 months after treatment with fingolimod and there was complete resolution of ME after discontinuing the medication. This finding was shown on the OCT in our patient. Early detection of the visual symptoms and discontinuation of the medication helps in the fast resolution of ME.

We recommend the regular screening for the MS patients treated with fingolimod with Amsler grid, fundus examination, and OCT study for documenting the macular edema.

Conflicts of interest None.

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