Resolution of Vacuole in Central Serous Chorioretinopathy Following Intravitreal Bevacizumab Injection

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ABSTRACT

We aimed to present a patient with complete resolution of the vacuole sign, which is a previously defined optical coherence tomography (OCT) finding of central serous chorioretinopathy (CSC), after injection of intravitreal bevazicumab (IVB). A 38-year old male patient presented with the complaint of decreased vision in the left eye. Fundus examination revealed well-defined diffuse serous retinal detachment in the macula of the left eye and the OCT section through that area revealed a serous detachment area, hyper-reflective fibrinous material accumulation and two vacuolar structures visible as hyporeflective spaces. In this coexistence of the findings, a recurrent CSC episode accompanied by fibrin accumulation was considered and an IVB injection was performed. One month later, OCT revealed complete resolution of the subretinal fluid and vacuole sign in addition to irregularities in RPE and the ellipsoid zone. IVB injection may be used as an effective treatment in CSC associated with fibrin accumulation and could have an important role in the resolution of the vacuole sign which consists of fibrin accumulation.

Keywords: Central serous chorioretinopathy, Intravitreal bevacizumab, Vacuole sign.

INTRODUCTION

Central serous chorioretinopathy (CSC) is a chorioretinal disease, predominantly affecting middle-aged males and is characterized by serous retinal detachment generally affecting the macular area and is associated with focal pigment epithelial detachment (PED).[1] The exact pathophysiology of CSC remains unclear, but abnormalities in inner choroidal layers such as venous congestion, ischemia and/or inflammation lead to choroidal hyperpermeability, secondary retina pigment epithelium (RPE) damage and serous detachment of the neural retina.[2]

Optical coherence tomography (OCT) is the gold standard technique in the diagnosis and monitoring of CSC. OCT reveals various pathological changes such as serous retinal detachment, PED, subretinal deposits, RPE atrophy, and brush-border pattern in patients with CSC, and the vacuole sign has been previously defined.[3-5]

Vascular endothelial growth factor (VEGF) is produced by retinal and choroidal cells and VEGF increases vascular permeability and edema by uncoupling endothelial cell to cell junctions.[6] Therefore, anti-VEGF agents are used therapeutically to reduce or reverse the choroidal leakage in acute CSC.[7] Intravitreal bevacizumab (Avastin, Roche, Welwyn GardenCity, UK) (IVB), which is a humanized monoclonal antibody to VEGF, has demonstrated favorable outcomes without serious adverse effects in patients with CSC.[7,8]

The case is here reported of a patient with complete resolution of the vacuole sign, which is an OCT finding of CSC, after injection of a single dose of IVB.

CASE REPORT

A 38-year old male patient presented with complaints of blurred vision and decreased visual acuity in the left eye. The patient had no systemic problems and did not report any chronic drug use. There was no history of ocular trauma or surgery. The patient had previously reported similar blurred vision complaints that lasted for 2 months and these complaints had resolved spontaneously without any medication or treatment. After the first episode the patient had not experienced any blurred vision for approximately 6

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months, and these current complaints of blurred vision and decreased visual acuity had been present for approximately 3 months. The best corrected visual acuity (BCVA) was 20/20 in the right eye and 20/100 in the left eye. Intraocular pressures were within normal limits in both eyes. Anterior segment examinations of both eyes were unremarkable. Dilated fundus examination demonstrated that while the posterior segment of the right eye was completely normal, in the left eye there was a well-defined diffuse serous retinal detachment, a yellowish subretinal fibrinous material accumulation adjacent to the fovea, and a darker spot within the yellowish fibrin (Figure 1). In the early phase of the FFA in the left eye, the point of leakage in the RPE was seen as hyperfluorescence, and atrophic areas as a result of previous attacks were hyperfluorescent. In the late phase, the hyperfluorescence at the active leakage point did not change and the serous retinal detachment area became more prominent (Figure 2). The vertical and horizontal spectral domain OCT section through the area of fibrinous material revealed serous detachment, hyper-reflective fibrinous material accumulation extending from the RPE to the subretinal area within the detachment area, and two vacuolar structures visible as hyporeflective spaces amid the hyper-reflective fibrin (Figure 3). Central macular thickness (CMT) was 213 μm in the right eye and 430 μm in the left eye. With this coexistence of the findings, a recurrent CSC episode accompanied by fibrin accumulation was considered and IVB injection was recommended for the left eye of the patient. Written informed consent was obtained from the patient for the off-label use of bevacizumab after the explanation of the potential complications of such a treatment. The IVB injection was performed under sterile conditions in the operating room. After applying topical tetracaine 1%, the periocular skin and eyelid and eyelashes were applied with povidone-iodine 10%. An eyelid speculum was then inserted and the ocular surface and fornices were rinsed with 1-2 drops of povidone-iodine 5% for 3 minutes. An intravitreal injection of 2.5 mg (0.1 ml) bevacizumab was administered using a 30-gauge needle. One month later, the BCVA improved to 20/32 in the left eye, and the OCT revealed complete resolution of the subretinal fluid and vacuole sign in addition to irregularities in RPE and the ellipsoid zone (Figure 4). CMT decreased to 172 μm. In the fundus autofluorescence imaging before and after IVB injection, the hyperautofluorescence field corresponding to the CSC area was seen to be granular hyperautofluorescence pattern after treatment (Figure 5). One month after the injection of IVB, the FFA of the left eye showing the areas of hyperfluorescence with no leakage compatible with the window defect pattern (Figure 6). After three and six months, the BCVA was maintained and the OCT and FFA images were similar to those at 1 month post-injection (Figure 7). No subretinal fluid was observed in the final follow-up examination and the BCVA was preserved CMT was 182 μm. Intraocular pressure was normal throughout the follow-up period.

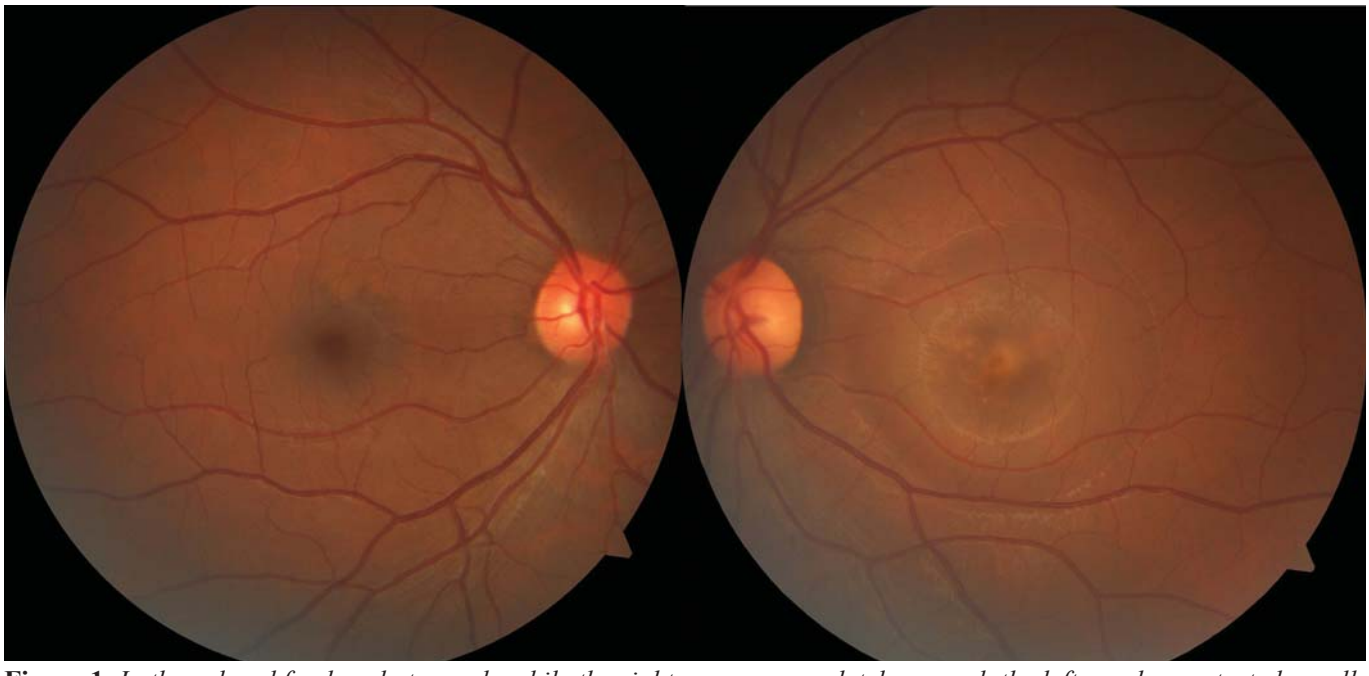

Figure 1. *In the colored fundus photograph, while the right eye was completely normal, the left eye demonstrated a well-defined diffuse serous retinal detachment area, a yellowish subretinal fibrinous material accumulation adjacent to the fovea, and a darker spot within the yellowish fibrin.*

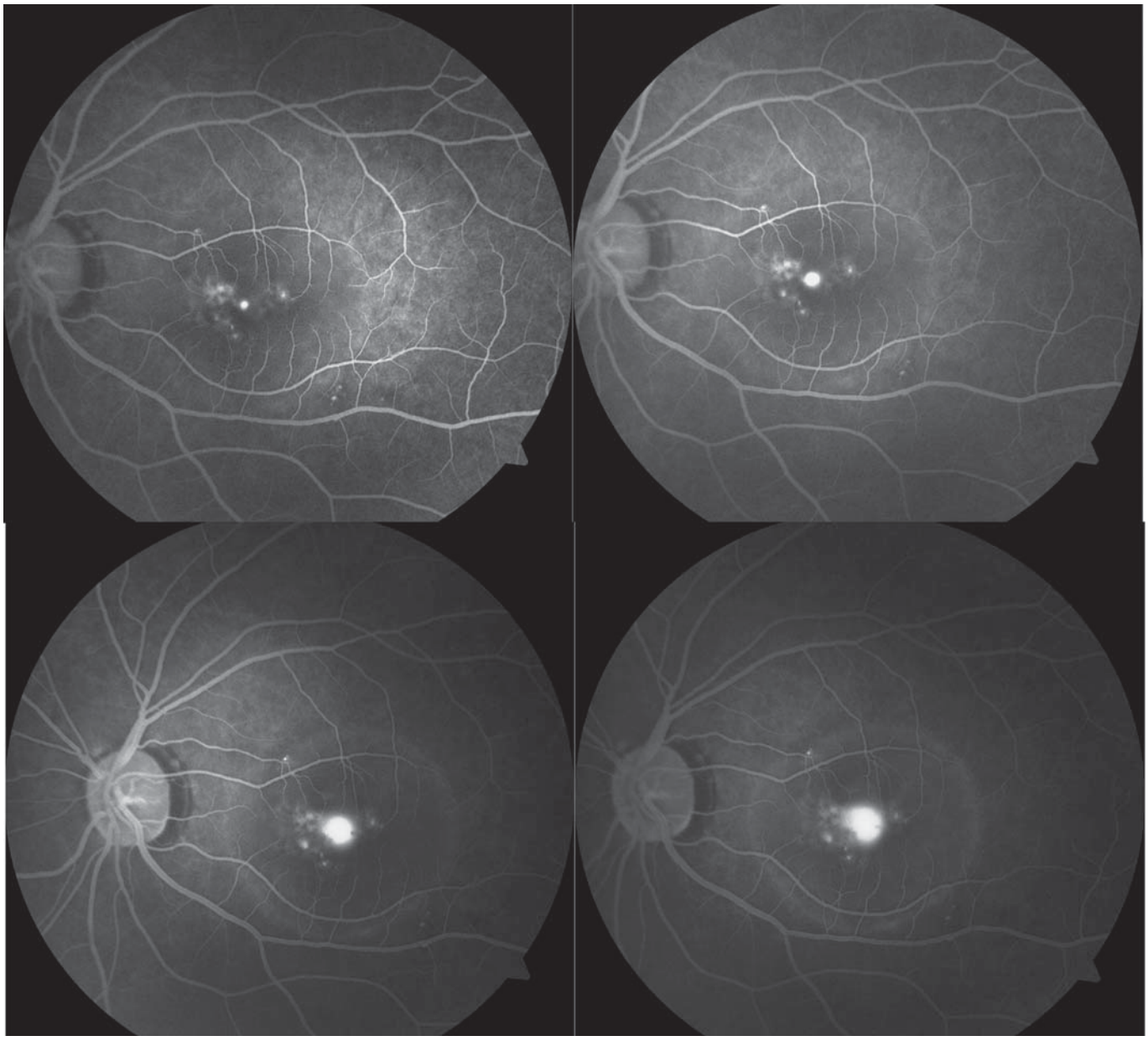

Figure 2. *In the early phase of the FFA, the point of leakage in the RPE was seen as hyperfluorescence, and atrophic areas as a result of previous attacks were hyperfluorescent. In the late phase, leakage of the fluorescein into the subretinal space is visible.*

DISCUSSION

CSC generally shows spontaneous resolution within 3-4 months with an overall good visual outcome.[9] However, recurrences are possible in up to 50% of patients within the first year and for several years after the first episode.[9] After recurrences, CSC can be a destructive disease and these recurrences or chronic neurosensory detachments may lead to RPE atrophy or hypertrophy with irreversible loss of visual function.[10]

Optic coherence tomography has an important role in the diagnosis and follow-up of CSC. Several OCT studies have demonstrated hyper-reflectivity in the subretinal space corresponding to the fibrin material and have also demonstrated dipping of the neurosensory retina at the site of fibrin formation.[11,12] Sometimes, this fibrin accumulation has hyporeflective areas and has been named the vacuole sign.[4,5] Rajesh et al.[5], reported that the presence of a hyporeflective vacuole amid the hyper-reflective fibrin adjacent to RPE defects probably indicates the site of constant fluid egress. They also emphasized that the sign could be an important indicator of disease activity, especially in cases where FFA is not possible.[5] In the current case, regression of the vacuole sign resulted in favorable improvements in visual acuity. The resolution of that sign might be an indicator of response to treatment and could also be a prognostic factor.

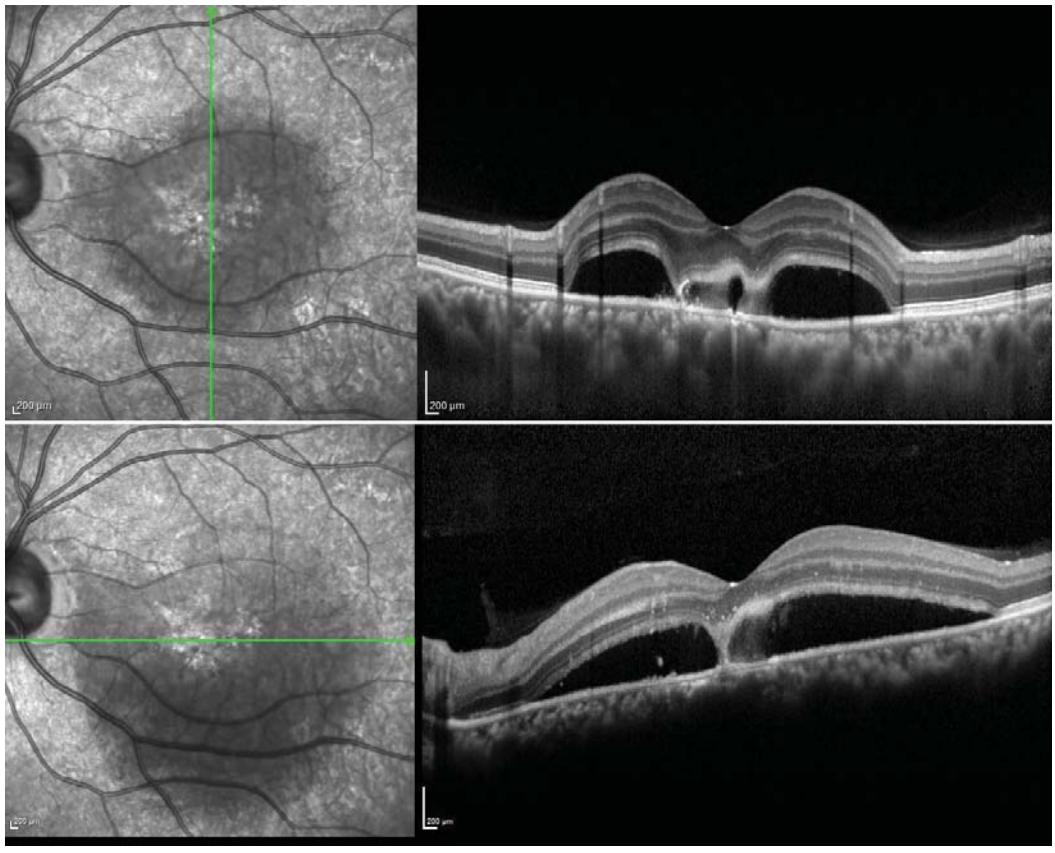

Figure 3. *The vertical and horizontal OCT section through the area of fibrin revealing serous detachment, hyper-reflective fibrinous material accumulation extending from the pigment epithelium to the subretinal area within the detachment area, and two vacuolar structures visible as hyporeflective spaces.*

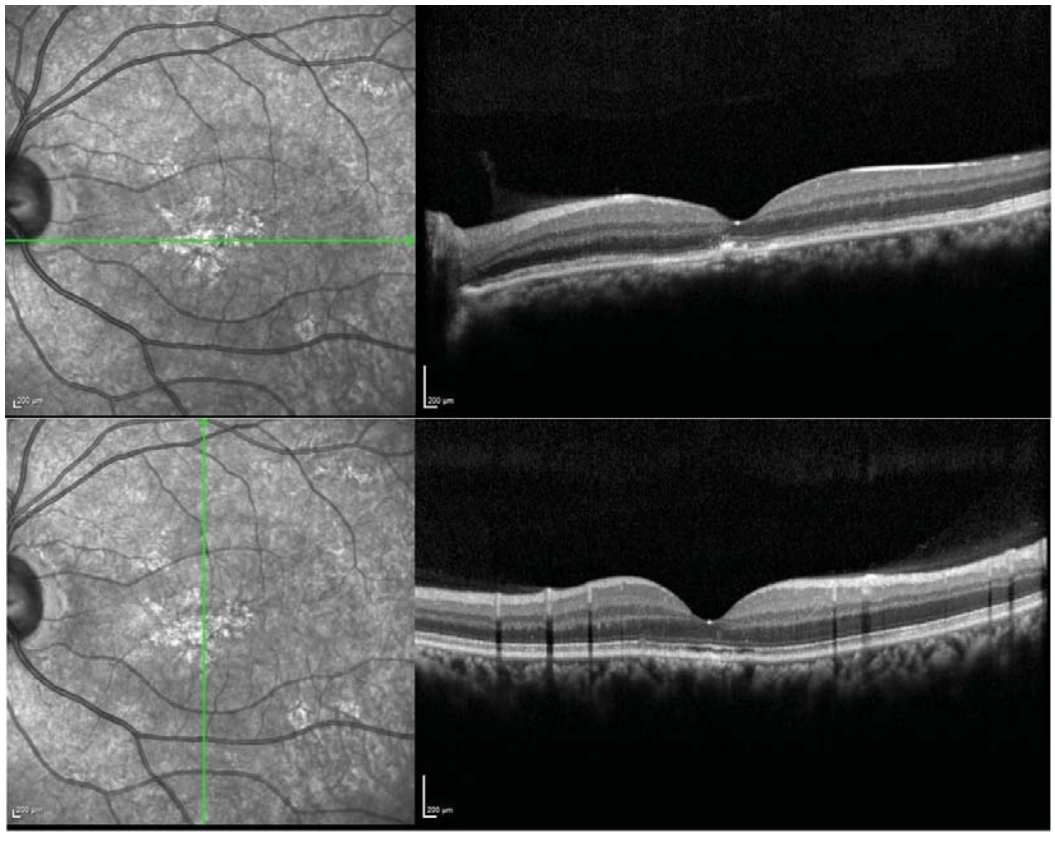

Figure 4. *One month after the injection of IVB, the OCT of the left eye demonstrating completely resolution of the subretinal fluid and vacuole sign in addition to irregularities in RPE and ellipsoid zone.*

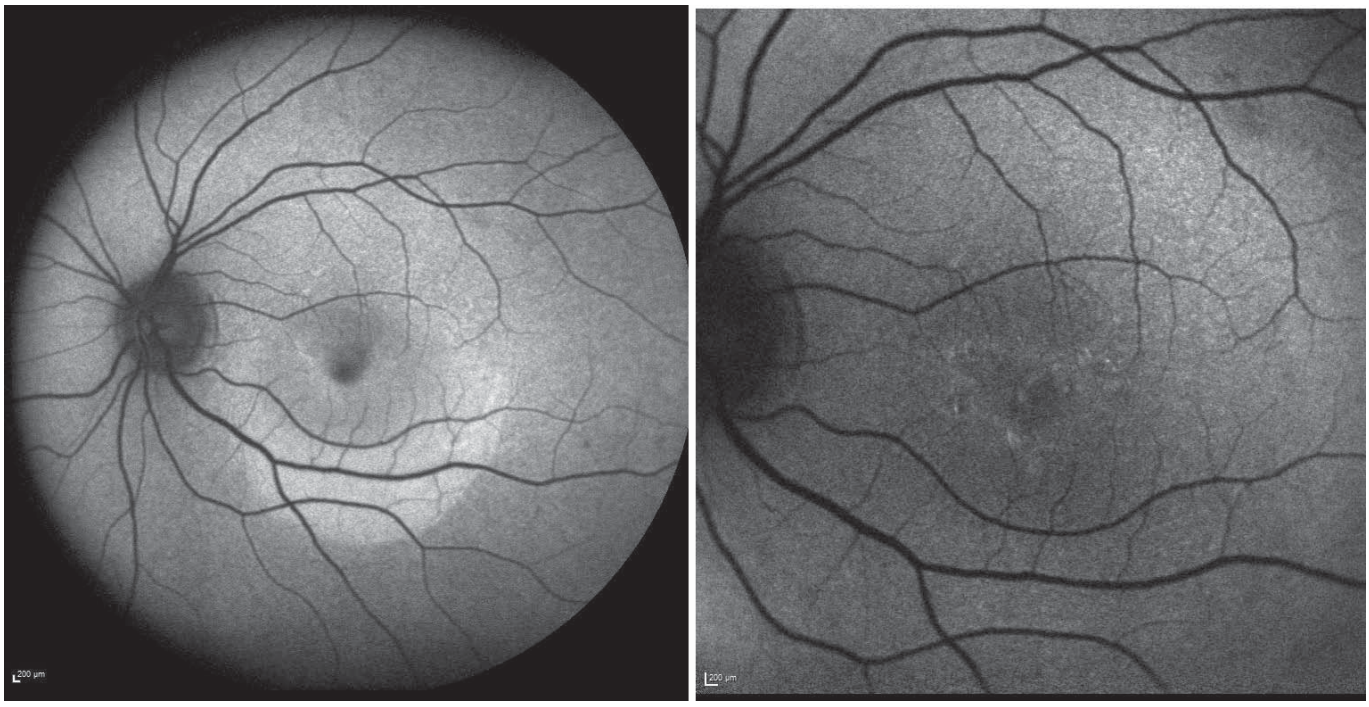

Figure 5. *In the fundus autofluorescence imaging before and after IVB injection, the hyperautofluorescence field corresponding to the CSC area was seen to be granular hyperautofluorescence pattern after treatment.*

There are different modalities of treatment for CSC. Observation can be regarded as a first-line approach in newly-diagnosed cases of less than 3 months duration.[13] Other treatment options include focal laser photocoagulation, micropulse diode laser photocoagulation, photodynamic therapy, anti-VEGF agents, anti-corticosteroids, adrenergic blockers and systemic carbonic anhydrase inhibitors.[13-15] These treatments are reserved for chronic CSC, recurrent CSC, single CSC attack of more than 3 months duration, and if the fellow eye has suffered permanent visual loss due to a previous episode of CSC, whether acute or chronic. IVB has been reported to be effective in CSC patients with symptoms lasting longer than 3 months.[7,8] It has been reported that repeated IVB administration can be considered a useful treatment option for recurrent CSC when patients have previously responded well to the same therapy.[16] In addition, a VEGF-related pathophysiological mechanism may be involved in the development of CSC. Recently, Baek and Park[17] reported that the optical density of subretinal fluid may be different between CSC and polypoidal choroidal vasculopathy. Therefore, Shin et al.[16] postulated that the subretinal fluid may be more turbid in cases of CSC with a VEGF-dependent mechanism than in those without a VEGF-dependent mechanism.[1] The current patient presented after a second episode of CSC and fibrin accumulation was observed on the OCT images. This patient was keen to receive this treatment because of occupational needs and excessive discomfort caused by the decreased vision. Therefore, the patient was treated with a single dose IVB injection and the BCVA improved in addition to complete resolution of the subretinal fluid and the vacuole sign one month after the injection. To the best of our knowledge, this is the first reported case in literature of resolution of the vacuole sign after IVB injection.

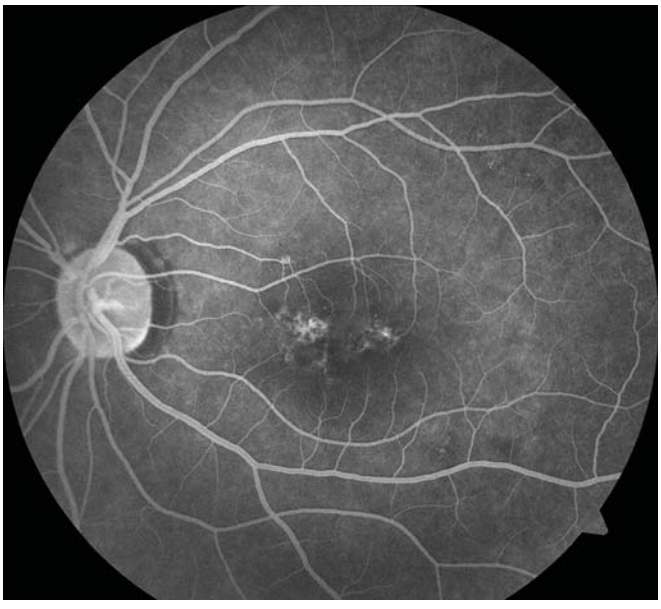

Figure 6. *One month after the injection of IVB, the FFA of the left eye showing the areas of hyperfluorescence with no leakage compatible with the window defect pattern.*

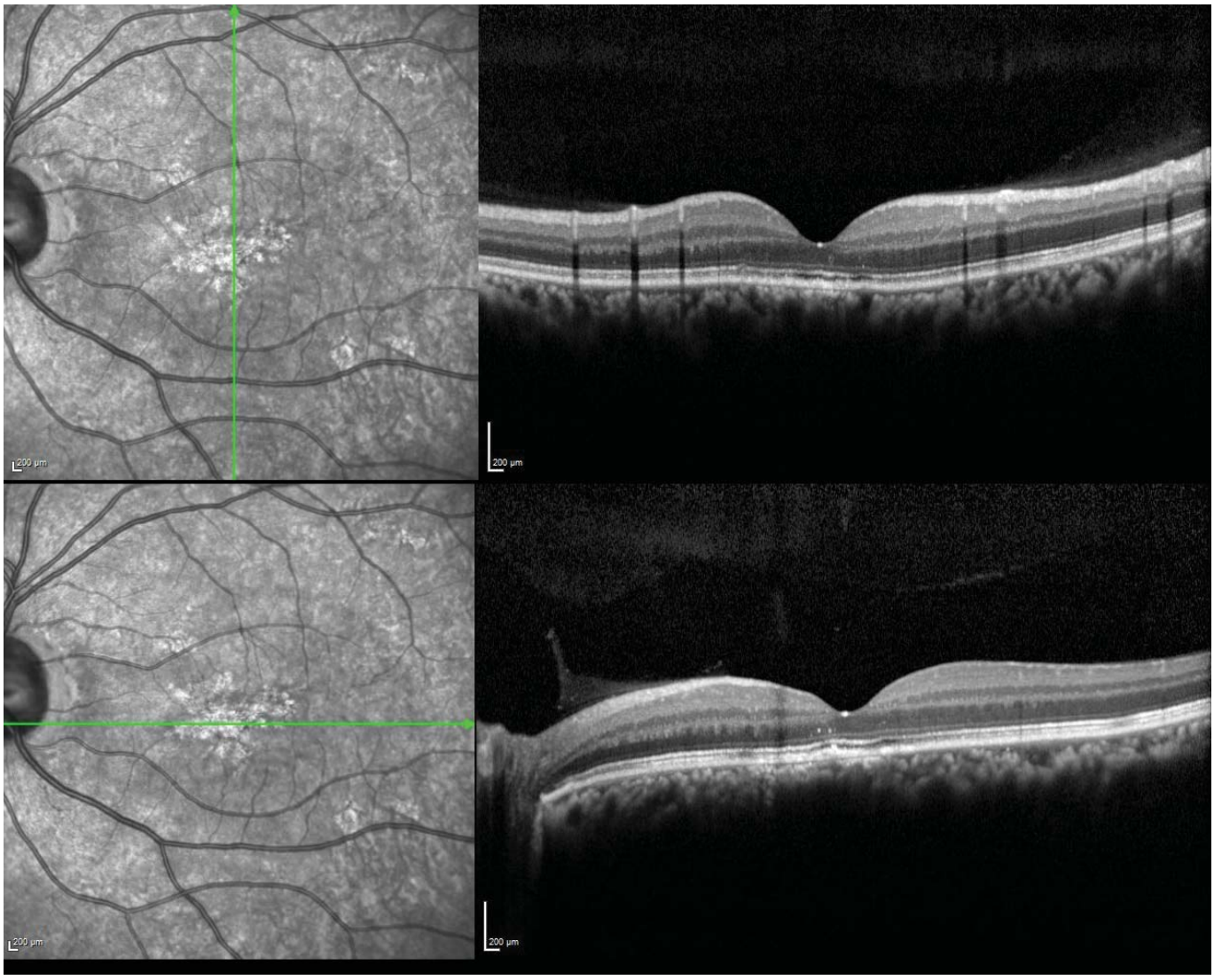

Figure 7. *No subretinal fluid was observed on OCT at six months post-injection.*

In conclusion, the vacuole sign is a previously defined OCT finding of CSC and could be an important sign of disease activity. IVB injection may be used as an effective treatment in CSC associated with fibrin accumulation and may have an important role in the resolution of the vacuole sign, which consists of fibrin accumulation.

Ethics

Informed Consent: It was taken from patient or legal guardians.

Conflict of Interest: No conflict of interest was declared by the authors.

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