



Atypical Chronic Central Serous Chorioretinopathy Mimicking Vogt-Koyanagi-Harada Disease: Full Therapeutic Response to Half-Fluence Photodynamic Therapy

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Abstract

The aim of this case report is to describe a case of atypical central serous chorioretinopathy (CSCR) definitively diagnosed after 8 years. A 44-year-old woman presented with reduced visual acuity in her left eye. Her visual acuity was light perception with projection in the right eye and 0.15 in the left. She described a similar decline in vision in her right eye 8 years ago. At that time, she had exudative retinal detachment and was treated with systemic immunosuppressive therapy for a presumed diagnosis of Vogt-Koyanagi-Harada disease. Despite resolution of the exudative retinal detachment, macular scarring developed. Eight years later, she developed inferior exudative retinal detachment in the left eye. A diagnosis of atypical CSCR was made with the help of multimodal imaging and her left eye was successfully treated with eplerenone and half-fluence photodynamic therapy (hf-PDT). In conclusion, early diagnosis and treatment of atypical CSCR may prevent subretinal fibrosis formation and permanent vision loss. Hf-PDT and eplerenone are successful treatment options for atypical CSCR.

Keywords: Atypical central serous chorioretinopathy, indocyanine green angiography, photodynamic therapy, eplerenone

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Introduction

Central serous chorioretinopathy (CSCR) is characterized by neurosensory macular detachment. However, in rare instances, the neurosensory detachment may be very extensive, causing bullous exudative retinal detachment. This rare variant of the disease is defined as atypical (bullous) CSCR. Characteristic fundoscopic features are multifocal exudative lesions in the posterior pole and inferior retinal detachment with shifting subretinal fluid.¹

Due to the unusual presentation, this form may be incorrectly diagnosed as rhegmatogenous retinal detachment, Harada disease, uveal effusion, multifocal choroiditis, metastatic carcinoma, or lymphoma.² Inappropriate use of systemic corticosteroids and other immunosuppressive agents may cause exacerbation of the symptoms and lead to development of subretinal fibrosis and scarring.

Case Report

A 44-year-old woman presented in 2019 because of a gradual decrease in vision in her left eye. Best corrected visual acuity (BCVA) was light perception with projection in the right eye and 0.15 Snellen line in the left eye.

Her previous medical records revealed a similar progressive reduction of vision in her right eye 8 years ago. At that time, in 2011, visual acuity in her right eye decreased to 0.15 Snellen line within a month, while BCVA in the left eye was 1.0 Snellen line. Anterior segment biomicroscopy was unremarkable. Fundoscopy showed trace vitreous cells and inferior exudative retinal detachment involving the macula of the right eye (Figure 1a). Optical coherence tomography (OCT) showed subretinal fibrotic material (Figure 1b). Fluorescein angiography showed central irregular hyperfluorescence in the macula surrounded by a hypofluorescent area caused by the blockage of subretinal fibrotic material and window defects from the areas of diffuse retinal pigment epithelium (RPE) alterations (Figure 1c). A full diagnostic work-up was planned. Infectious markers were negative. Consultations with the departments of pulmonary diseases and neurology were requested to exclude tuberculosis, sarcoidosis, and neurological signs of Vogt-Koyanagi-Harada (VKH) syndrome. With a preliminary diagnosis of VKH disease, intravenous pulse corticosteroid therapy (250 mg methylprednisolone sodium succinate infusion 4 times a day) was given for 3 days, followed by oral prednisolone 60 mg/day tapered by 10 mg per week. Oral cyclosporine A at a dose of 200 mg/day was also prescribed. At 2 months, her BCVA decreased to counting fingers at 20 cm and exudative detachment progressed (Figure 1d). In addition, BCVA in her left eye decreased to 0.4 Snellen line due to acute-onset inferior retinal detachment. At this point, sight-threatening corticosteroid-resistant VKH disease was suspected and treatment with infliximab infusion at a dose of 5 mg/kg was initiated and applied every 4 weeks thereafter. After 6 monthly infliximab infusions, her BCVA was counting fingers at 20 cm in her right eye and 0.9 Snellen line in her left eye. Exudative retinal detachment completely

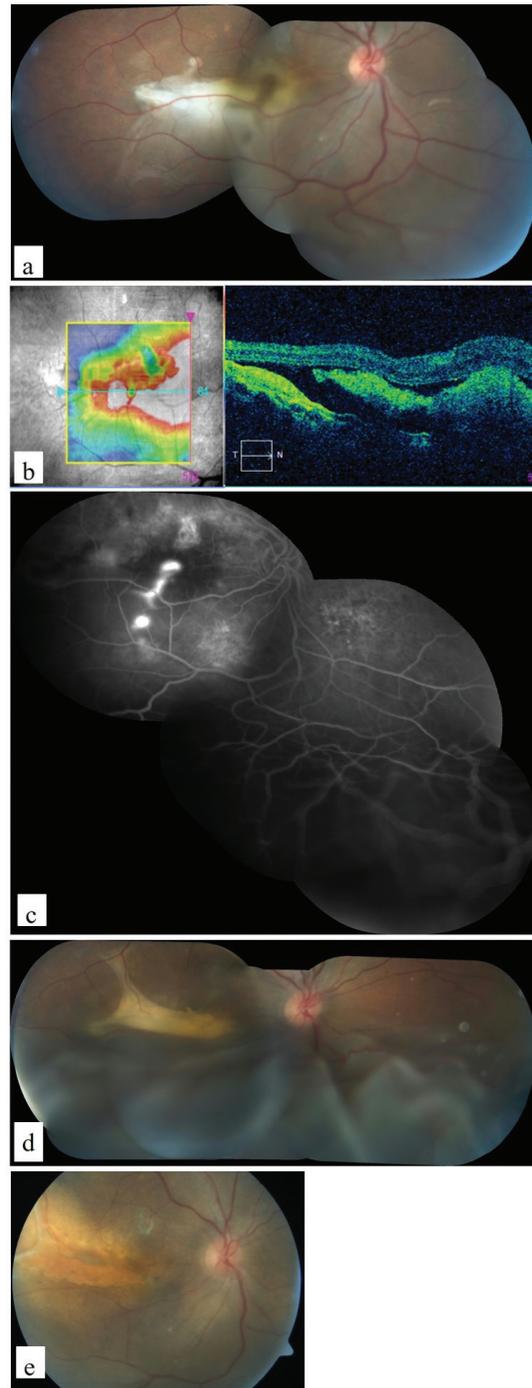


Figure 1. Multimodal retinal images obtained during initial involvement of the right eye: a) Color fundus photography revealed exudative retinal detachment involving the posterior pole and yellowish subretinal fibrin located at the macula. b) Optical coherence tomography showed the presence of subretinal fibrin along with subretinal fluid. c) Fluorescein angiography showed central irregular hyperfluorescence in the macula surrounded by a hypofluorescent area caused by the blockage of subretinal fibrotic material and window defects from the areas of diffuse retinal pigment epithelium alterations. d) Color fundus photography revealed the progression of exudative retinal detachment and yellowish fibrinous material in the macula of the right eye. e) Color fundus photography demonstrated complete regression of the exudative retinal detachment with atrophy and scarring in the macula after 8 months

regressed in both eyes. However, a centrally located macular scar and subretinal fibrotic bands remained as a sequel of the previous detachment in her right eye (Figure 1e). Infliximab therapy was discontinued and follow-up visits were scheduled every 3 months. Forty-four months after cessation of treatment, OCT revealed multiple serous pigment epithelial detachments without subretinal fluid in her left eye (Figure 2). At that time, her BCVA was light perception with projection in the right eye and 1.0 Snellen line in the left eye. Follow-up visits were extended to every 6 months.

In 2019, 98 months after initial presentation, she presented with decreased vision in her left eye. Her visual acuity was 0.8 Snellen line in her left eye and there was acute-onset inferior exudative retinal detachment. Infliximab infusions (5 mg/kg) were planned for week 0, 2, 6, and every 8 weeks thereafter. Oral azathioprine (125 mg/day) was also prescribed. After 2 doses of infliximab, her BCVA decreased to 0.15 Snellen line, and the detachment fluid in the posterior pole increased. Fluorescein angiography (FA) showed multiple leakage points and retinal pigment epithelial alterations, while indocyanine green angiography revealed areas of choroidal hyperpermeability (Figure 3). Based on these imaging findings, the patient was diagnosed with atypical CSCR. All treatments were ceased, and an oral mineralocorticoid receptor antagonist, eplerenone (Inspra®, Pfizer Pharmaceuticals LLC, Vega Baja, Puerto Rico), was initiated at a dose of 25 mg twice daily. A half-fluence

photodynamic therapy (hf-PDT) protocol (25 J/cm², 300 mW/cm²) using 6 mg/m² intravenous verteporfin (Visudyne®, Novartis, JHP Pharmaceuticals LLC, MI, USA) was applied to the areas of leakage and hyperpermeability in the inferior papillomacular region seen in combined FA and ICGA images. At 1 month after hf-PDT, subretinal fluid was markedly decreased, serous pigment epithelial detachment had regressed, and choroidal thickness was reduced (Figure 4). Visual acuity in her left eye was 0.16 ETDRS line. After 6 months, the inferior exudative retinal detachment had fully regressed and her visual acuity increased to 0.5 ETDRS line. Eplerenone therapy was discontinued. At 1 year after hf-PDT, her BCVA was light perception in the right eye and 0.63 ETDRS line in the left eye, with no recurrence of exudative retinal detachment and a completely dry macula (Figure 5).

Discussion

The pathogenesis of CSCR is not well documented. A breakdown in the permeability of the choriocapillaris has been implicated as the possible pathogenetic mechanism, leading to a focal loss of RPE-Bruch's membrane attachment and allowing passage of the choroidal fluid into the subretinal space.³ Bullous retinal detachment is an extremely rare atypical variant of chronic CSCR which has been reported in a limited number of case presentations and case series.^{1,4}

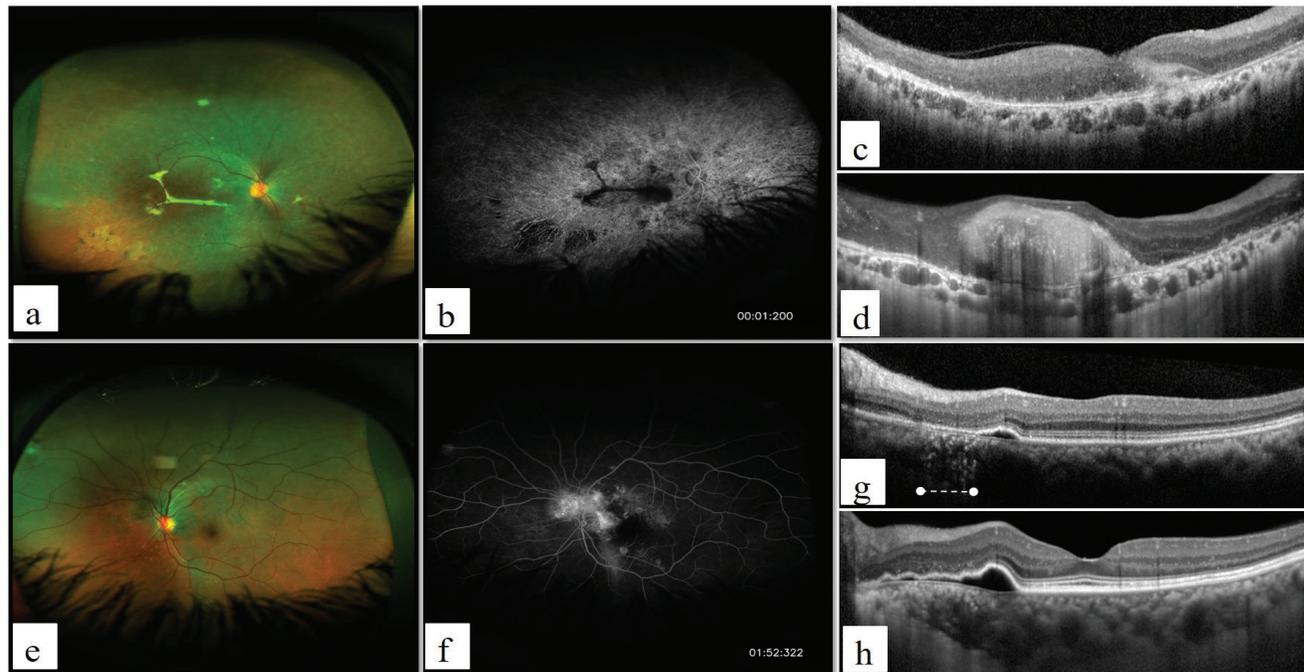


Figure 2. Multimodal fundus images of both eyes at 52 months after first presentation. Right eye: a) Ultra-widefield color fundus photography showed fibrinous scar at the posterior pole and inferotemporally located areas of atrophy. b) Early-phase fluorescein angiography (FA) revealed window defects due to diffuse retinal pigment epithelium (RPE) alterations, blockage by the fibrinous scar, and increased visibility of the choroidal vessels in the atrophic areas. c) Optical coherence tomography (OCT) showed complete retinal pigment epithelium and outer retinal atrophy (RORA). d) Enhanced depth imaging mode OCT (EDI-OCT) showed dense fibrinous scar in the macula, diffuse RPE loss, and dilated Haller layer vessels with prominent attenuation of the choriocapillaris layer. Left eye: e) Ultra-widefield color fundus photography showed grayish area located at the superior peripapillary region. f) Early-phase FA revealed peripapillary window defects due to RPE alterations and hyperfluorescent gravitational tract. g) OCT showed barcode sign (dashed line) due to incomplete RORA. h) EDI-OCT showed serous pigment epithelial detachment and increased choroidal thickness

Corticosteroid therapy is one of the many systemic factors implicated in the pathogenesis of the bullous variant of CSCR.⁴ In our case, due to the presence of trace amount of vitreous cells, the patient was initially misdiagnosed with VKH disease and received intravenous high-dose corticosteroids. The use

of steroids may aggravate the clinical findings of CSCR. Then, because the patient's findings did not improve and her vision worsened, steroid-resistant VKH was suspected and her treatment was changed to other immunosuppressive and biologic agents.⁵

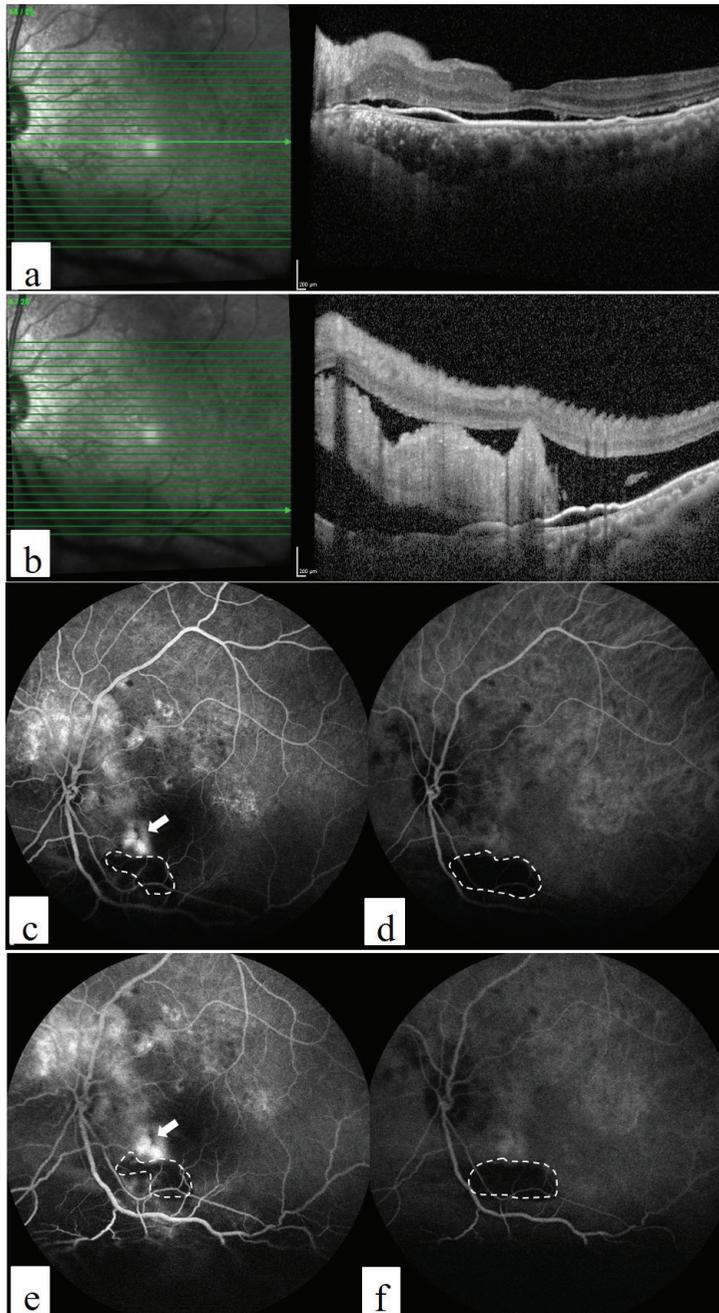


Figure 3. Multimodal retinal images obtained during latest activation in the left eye. a) Optical coherence tomography (OCT) showed subretinal fluid, serous pigment epithelial detachment, and increased choroidal thickness. b) Inferior section of OCT showed dense hyperreflective fibrotic material in the subretinal area and increased amount of subretinal fluid. Combined dye angiography images of the left eye: c) Early-phase fluorescein angiography (FA) revealed peripapillary window defects, a hypofluorescent area due to the blockage by the subretinal fibrotic material (dashed circle), and an active leakage point (arrow). d) Early-phase indocyanine green angiography (ICGA) showed dilated choroidal vessels, areas of choroidal hyperpermeability, and a hypocyanescent area due to blockage by the subretinal fibrotic material (dashed circle). e) Late-phase FA revealed increased hyperfluorescence at the side of active leakage (arrow) and hypofluorescence due to blockage by the subretinal fibrotic material (dashed circle). f) Late-phase ICGA showed hypercyanescent areas of choroidal hyperpermeability and an area of hypocyanescent due to blockage by the subretinal fibrotic material (dashed circle)

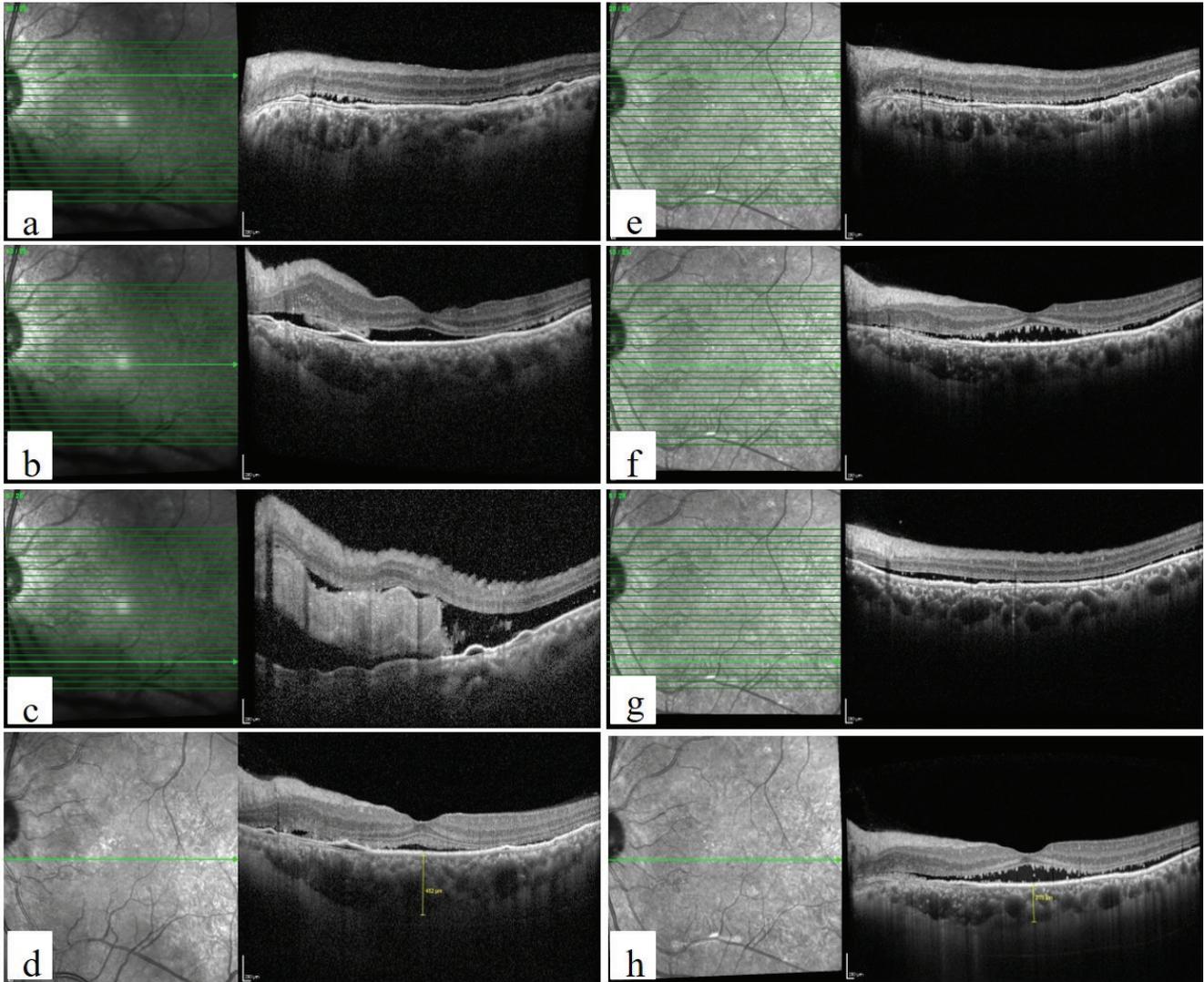


Figure 4. B-scan and enhanced depth imaging mode optical coherence tomography images passing through the same horizontal cross-sections before (a-d) and after (e-h) half-fluence photodynamic therapy. a-c) Increasing amount of subretinal fluid towards the inferior sections. c) Dense hyperreflective fibrinous material. d) Thick choroid, 452 μm . e-g) Regressed subretinal fluid. g) Loss of hyperreflective fibrinous material. h) Decreased choroidal thickness, 275 μm

In atypical CSCR cases, providing an earlier definitive diagnosis may be a clinical challenge. Atypical bullous CSCR is most commonly misdiagnosed as the acute phase of VKH due to the exudative retinal detachment.⁶ Subretinal fibrin reaction and presence of generalized RPE irregularities in the absence of vitreous cells and lack of optic disc hyperemia and edema are signs in favor of CSCR. An absence of optic disc staining on FA and ICGA is a finding that further facilitates the diagnosis of CSCR. On OCT, RPE bulge may be seen in CSCR, whereas RPE folds, fluctuations of the internal limiting membrane, and subretinal septa are seen only VKH.⁷ Subretinal fibrin reaction is frequently encountered in eyes with bullous CSCR.⁸

Therapeutic options for atypical CSCR include laser photocoagulation, PDT, and oral mineralocorticoid receptor antagonists.⁹ The main mechanism of action of PDT is angio-occlusion leading to constriction of choroidal vessels and choroidal vascular remodelling.¹⁰ Therefore, it may be the most appropriate treatment approach, being effective on the direct pathogenesis. In our case, we used a combination of half-fluence PDT and eplerenone therapy, which provided very rapid and complete resolution of subretinal fluid without complications.

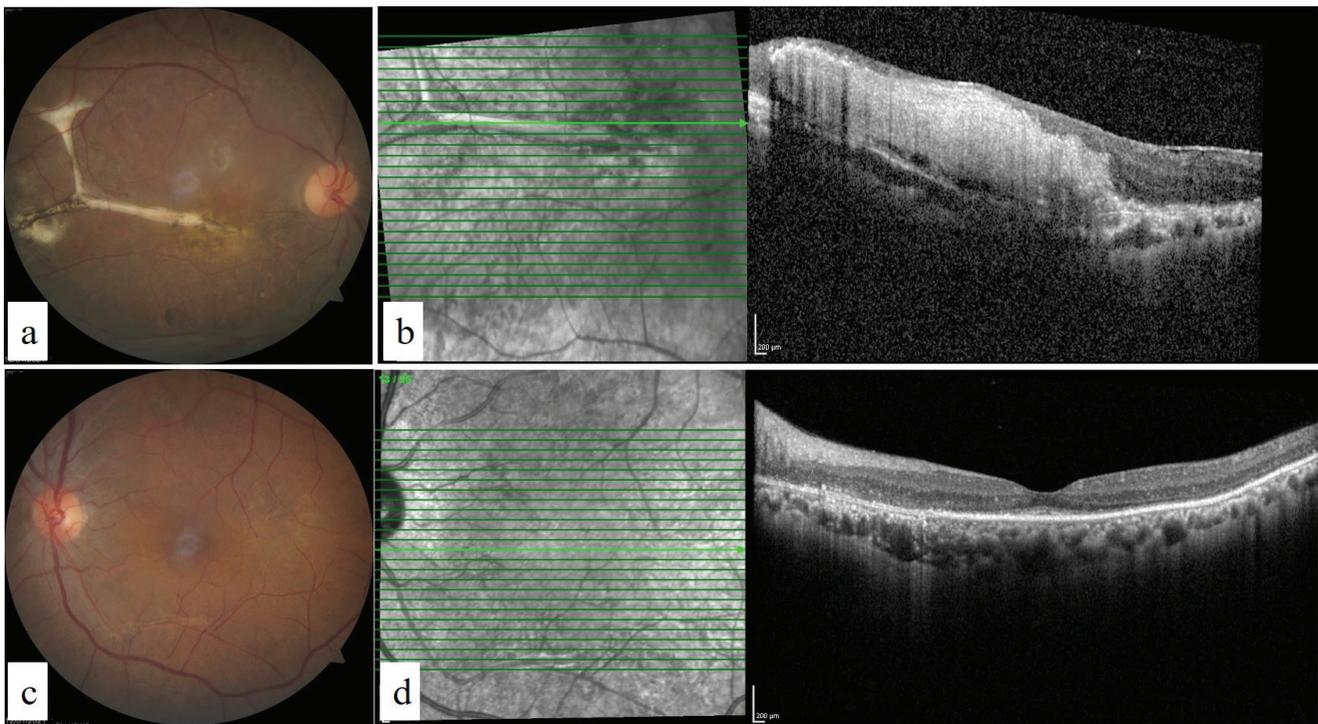


Figure 5. Color fundus photography and optical coherence tomography (OCT) images at the last visit: a) Color fundus photography of the right eye showed Y-shaped fibrinous scar with localized hyperpigmentation areas within it. b) OCT image of the right eye revealed dense fibrinous scar and epiretinal membrane formation. c) Color fundus photography of the left eye showed complete recovery. d) Optical coherence tomography of the left eye revealed loss of the external limiting membrane, ellipsoid and interdigitation zones, and disruption of the retinal pigment epithelium in the field of previous serous pigment epithelial detachment.

In conclusion, the use of multimodal imaging may enable early definitive differential diagnosis of atypical CSCR from other chorioretinal diseases. Otherwise, inappropriate use of corticosteroids and other immunosuppressive agents may worsen the clinical findings and lead to poor visual prognosis. Hf-PDT in combination with oral eplerenone may be a successful treatment option for atypical CSCR that prevents subretinal fibrosis and scar formation.

Ethics

Informed Consent: Obtained.

Peer-review: Externally peer reviewed.

Authorship Contributions

Surgical and Medical Practices: F.B., N.Y., Concept: Ö.Y., F.B., N.Y., S.D., E.Ö., Design: Ö.Y., F.B., N.Y., S.D., E.Ö., Data Collection or Processing: Ö.Y., Analysis or Interpretation: Ö.Y., F.B., N.Y., S.D., E.Ö., Literature Search: Ö.Y., F.B., N.Y., Writing: Ö.Y., F.B., N.Y., S.D., E.Ö.

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

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