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A case of bullous-variant of central serous chorioretinopathy in a patient with Goodpasture's disease

Case Presentation

A 46-year-old White female was diagnosed with Goodpasture's disease (GD) at age 22 via kidney biopsy. She was treated with oral corticosteroids and cyclophosphamide for two years, and has been taking an angiotensin-converting enzyme-inhibitor for the past several decades for nephroprotection. The patient has not required any additional immunosuppression, and has maintained normal kidney function outside of developing pre-eclampsia during pregnancy.

She endorsed increased stress recently, and presented with decreased visual acuity (VA) in the right eye to 20/50, while the left eye remained 20/20. The intraocular pressure, confrontational visual fields, extraocular motility, pupils, and anterior segment examination was normal in both eyes. Dilated fundus examination and optical coherence tomography (OCT) imaging demonstrated significant subretinal fluid (SRF) in the right eye (Figure 1). The SRF subsided and VA improved to 20/25 with observation in the right eye.

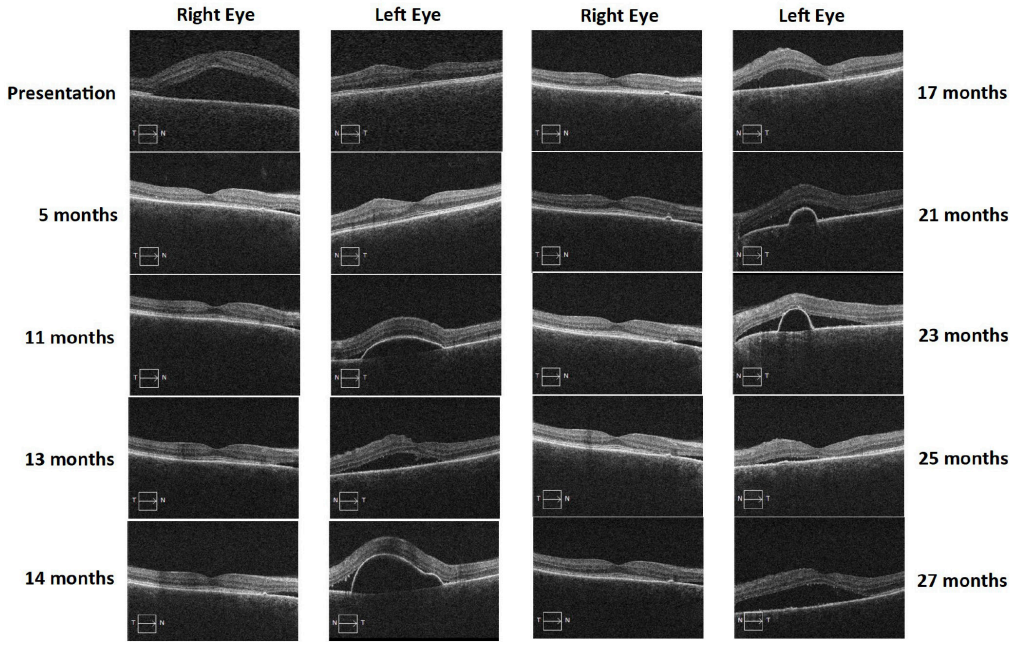

Figure 1: Optical coherence tomography of subretinal fluid fluctuation during follow-up.

Eleven months later, she presented with significant changes in vision in the left eye with VA decreased to 20/50. OCT showed trace SRF in the nasal macula in the right eye and a large pigment epithelial detachment (PED) with SRF in the left eye (Figure 1). Color and fundus autofluorescence (FAF) imaging of the right eye showed multifocal hypopigmented areas corresponding to the PED/SRF as well as hyperautofluorescent changes consistent with fluid guttering (Figure 2). On exam and fundus imaging, a large inferior exudative retinal detachment (RD) spanning from 2-10 o'clock was evident in the left eye (Figure 2). Fluorescein angiography (FA) revealed bilateral multifocal pooling and several scattered expansile dots in the macula, as well as a large active lesion along the inferior arcade in the left eye, which was likely responsible for the extensive subretinal exudation (Figure 3). Focal laser photocoagulation was applied to this lesion in hopes of inactivating it. In addition, although we initiated oral eplerenone after normal blood work results, the patient took pills inconsistently, and a decision was made to discontinue this therapy.

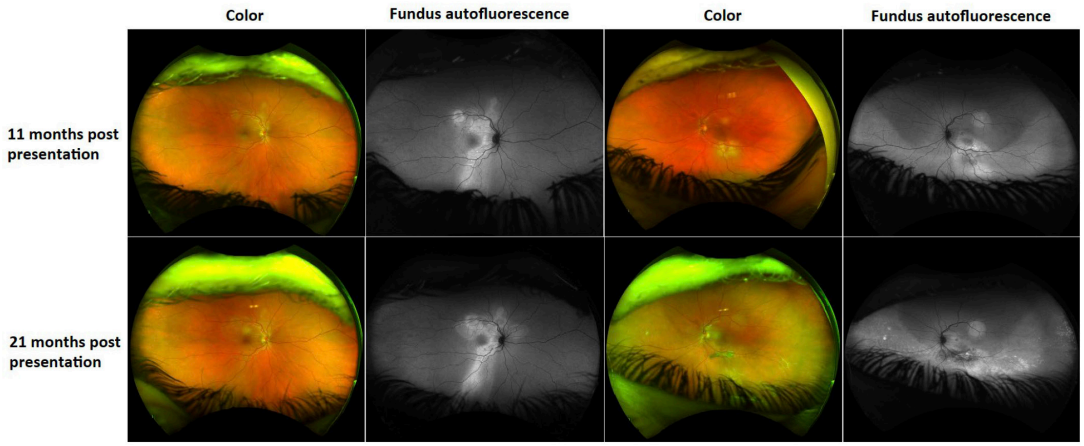

Figure 2: Optos color and fundus autofluorescence at 11 and 21 months after presentation.

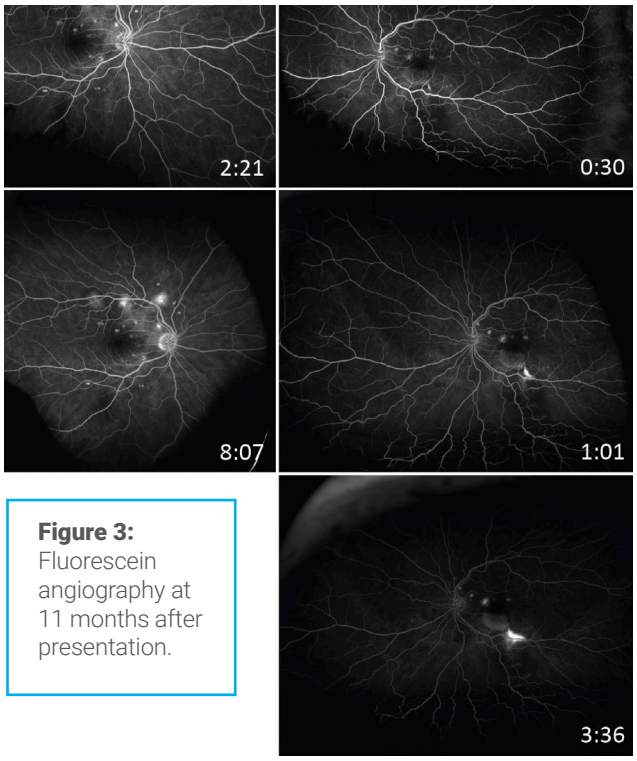

Figure 3: Fluorescein angiography at 11 months after presentation.

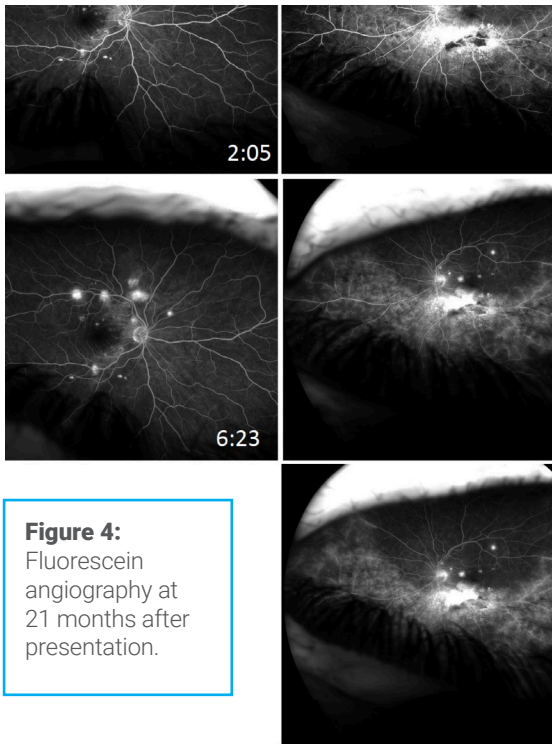

Figure 4: Fluorescein angiography at 21 months after presentation.

Fundus imaging 10 months later (21 months after presentation) showed a stable right eye, and a pigmented lesion along the inferior arcade from prior laser as well as a recalcitrant extensive exudative RD spanning from 1:30-10:30 o'clock with subretinal deposits in the left eye (Figure 2). FA showed multifocal pooling in the both eyes, with persistent inferior exudative RD in the left eye (Figure 4). In the left eye, the patient's SRF continued to show significant fluctuation throughout her clinical course (Figure 1). At final visit (30 months after the initial presentation), the OCT of the left eye showed multifocal serous PEDs with extensive proteinaceous, complex SRF, and diffuse intraretinal fluid (Figure 5). At this point, the VA was 20/40 in the right eye and 20/200 in the left eye. The patient was scheduled to undergo photodynamic therapy (PDT) at next visit.

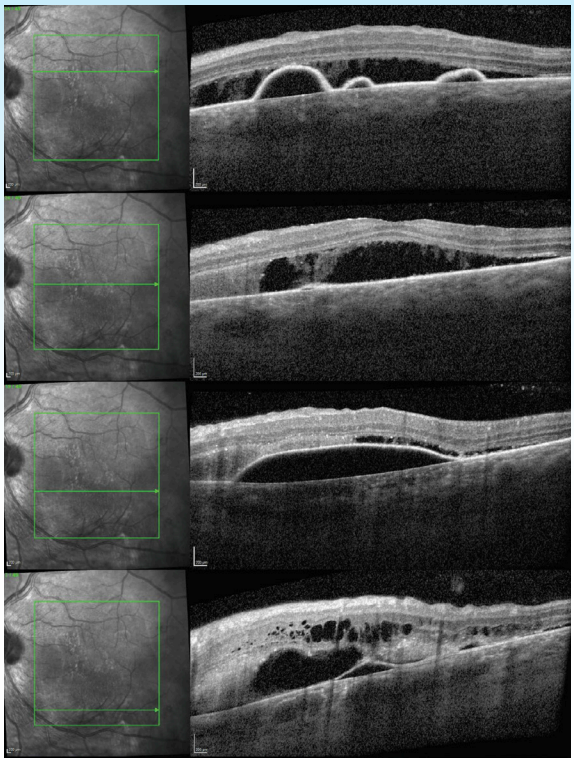

Figure 5: Optical coherence tomography of the left eye at final visit.

Discussion

Central serous chorioretinopathy (CSR) manifests as idiopathic subretinal and/or sub-retinal pigment epithelial (RPE) fluid, and can rarely present with bullous neurosensory RD.[1] This bullous variant of CSR (bvCSR) was first described by Gass in 1973, and is characterized by turbid subretinal sero-fibrinous exudate, multiple large PEDs, and multifocal leaks at the level of the RPE.[2] The differential diagnosis for bvCSR includes choroidal vasculopathies, infectious etiologies (e.g., syphilis, tuberculosis), inflammatory/autoimmune conditions (e.g., posterior scleritis, ulcerative colitis, Crohn's disease), systemic conditions (e.g., pituitary adenoma, hypoalbuminemia), malignancy (e.g., primary intraocular, metastases), and uveal effusion syndrome.[3-5]

Goodpasture's disease (GD) is a rare autoimmune small-vessel vasculitis, with a reported incidence between 0.5-1 cases per 1 million individuals per year.[6] It is an anti-glomerular basement membrane disease with pulmonary and renal manifestations due to autoantibodies against the non-collagenous 1 domain of type IV collagen.[7] Binding of antibodies to basement membrane antigens releases reactive oxygen species and activates the complement cascade.[8]

Ocular manifestations are uncommonly reported in patients with GD, but include serous RD (as in our patient);[9-11] subretinal neovascular membranes, retinal hemorrhages, and retinoschisis;[12] retinal vasculitis and macular edema;[13] as well as necrotizing scleritis.[14]

Systemic corticosteroid use, history of kidney disease, and autoimmune/rheumatoid diseases have been identified as significant risk factors for developing bvCSR.[15] Compared to patients with nonbullous CSR, patients with bvCSR are more likely to have bilateral disease and worse VA at diagnosis. In addition, OCT and FA findings in bvCSR more commonly include retinal folds, subretinal fibrin, multiple PEDs and RPE tears, multifocal leakage, terminal telangiectasia, and peripheral retinal non-perfusion.[15] Our patient had many of these at-risk characteristics and ocular findings.

Treatment challenges in bvCSR remain due to fluid chronicity, amount of subretinal fibrin, and underlying co-morbidities.[16] Options include diuretics/anti-hypertensives, PDT, focal laser, and anti-vascular endothelial growth factor injections, as well as pars plana vitrectomy associated with trans-scleral or internal drainage. Our patient did not show a significant sustainable clinical improvement either with oral eplerenone or focal laser.

In summary, our patient demonstrated an unusual case of chronic bvCSR in GD. As reported in the literature, these patients may be recalcitrant to typical treatment options and may have poor visual outcomes.

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Enrolling Studies:

Wet AMD

Edison

Opthea Coast: A Phase 3, Multicenter, Double-masked, Randomized Study to Evaluate the Efficacy and Safety of Intravitreal OPT-302 in Combination with Aflibercept, Compared with Aflibercept Alone, in Participants with Neovascular Age-related Macular Degeneration (nAMD)

Toms River

Opthea Shore: A Phase 3, Multicenter, Double-masked, Randomized Study to Evaluate the Efficacy and Safety of Intravitreal OPT-302 in Combination with Ranibizumab, Compared with Ranibizumab Alone, in Participants with Neovascular Age-related Macular Degeneration (nAMD)

Teaneck

Elevatum: A Phase IIIB/IV, Multicenter, Open-Label, Single-Arm Study to investigate Faricimab treatment in response to treatment-naïve, underrepresented patients with Diabetic Macular Edema

Teaneck

Luna: A Multi-Center, Randomized, Double-Masked Phase 2 Study to Assess Safety and Efficacy of ADVM-022 (AAV.7m8-aflibercept) in Anti-VEGF Treatment Experienced Patients with Neovascular (Wet) Age[1]related Macular Degeneration

Teaneck

DAVIO: A Phase 2, Multicenter, Prospective, Randomized, Double-Masked, Parallel Study of EYP-1901, a Tyrosine Kinase Inhibitor (TKI), Compared to Aflibercept in Subjects with Wet AMD

Diabetic Retinopathy

Teaneck

Ocuterra: A Phase 2 Randomized, Double-Masked, Vehicle[1] Controlled, Multicenter Study to Evaluate the Safety and Efficacy of OTT166 Ophthalmic Solution in the Treatment of Diabetic Retinopathy (DR)

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PAVIO: A Phase 2, Multicenter, Prospective, Double-masked, Parallel Study of EYP-1901, a Tyrosine Kinase Inhibitor (TKI), compared to Sham for the Improvement of Moderately Severe to Severe Nonproliferative Diabetic Retinopathy (NPDR)

Upcoming Studies:

GA / Dry AMD

Teaneck

Alexion: A Phase 2, Double-Masked, Placebo-Controlled, Dose Range Finding Study of Danicopan (ALXN2040) in Patients with Geographic Atrophy (GA) Secondary to Age-Related Macular Degeneration (AMD)

Janssen: Phase 2/3, Randomized, Double-masked, Multicenter, Dose-ranging, Sham[1]Controlled Clinical Trial to Evaluate Intravitreal JNJ-81201887 (AAVCAGsCD59) Compared to Sham Procedure for the Treatment of Geographic Atrophy (GA) Secondary to Age-related Macular Degeneration

RVO

Teaneck, Toms River, Edison

Bayer Study: A Randomized, Double-Masked, Active-Controlled, Phase 3 Study of the Efficacy and Safety of Aflibercept 8 mg With Macula Edema due to Retinal Vein Occlusion

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