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Case Report

Choroidal Neovascular Membrane Causing Vitreous Hemorrhage from Inactive Chorioretinal Scar due to a Case of Ocular Toxoplasmosis

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Abstract

We report a case of a choroidal neovascular membrane that developed from a chorioretinal scar in the setting of prior active Toxoplasma chorioretinitis. The patient initially presented as a referral for acutely blurry vision determined to be from a vitreous hemorrhage. She underwent a pars plana vitrectomy, which uncovered an inactive appearing chorioretinal scar. Subsequently, the patient developed a flare-up of Toxoplasma chorioretinitis that was confirmed by positive Toxoplasma polymerase chain reaction after a vitreous sample was obtained via vitreous tap. After the infection was appropriately managed, the patient developed new, albeit smaller, subretinal and preretinal hemorrhage determined to be from a choroidal neovascular membrane in the area of the chorioretinal scar. This bleeding was controlled successfully with multiple intravitreal injections of anti-vascular endothelial growth factor with return to the patient's baseline visual acuity.

Keywords: Choroidal neovascular membrane; Vitreous hemorrhage; Chorioretinal scar

Introduction

Choroidal Neovascularization (CNV) can be caused by many different pathologic processes, including degenerative, heredodegenerative, inflammatory, neoplastic, traumatic, and even idiopathic causes. In our patient, she experienced a non-documented case of ocular toxoplasmosis long before presenting to our clinic. In typical cases, Toxoplasma causes a foci of retinochoroiditis that appears as a yellow-white chorioretinal (CR) lesion with indistinct margins combined with an overlying severe vitritis (described as "a headlight in the fog"), which leads to the formation of a CR scar [1]. A Choroidal Neovascular Membrane (CNVM) then formed in the area of the scar in our patient, which eventually led to spontaneous bleeding resulting initially in a Vitreous Hemorrhage (VH) followed later by subretinal and preretinal hemorrhage. A CNVM is a late complication of ocular toxoplasmosis, mostly occurring in healed, inactive lesions and may be a cause of sudden loss of vision, especially in younger patients [2].

This case focuses on a 66 year old Korean female patient who presented to our teaching hospital eye clinic after she was referred from an outside hospital for acute vision changes of her right eye. Approximately 4 days prior to presentation, she began noticing many floaters, with progression to very blurry vision within less than 24 hours. At this time, she sought care at a local emergency department, and she was then referred to our eye clinic for ophthalmology evaluation. She denied further symptoms of flashes, seeing curtains/shadows, ocular pain or discharge, nor recent or past ocular trauma, but did endorse that the right eye felt itchy, red, and somewhat swollen. Her past medical history was significant for type II Diabetes Mellitus (DM-II). Her HbgA1c level was unknown and therefore her diabetic control status unclear at the time. Her past ocular history was significant for pseudophakia bilaterally and she endorsed being told that she had a scar in her right eye, but could not provide further details regarding etiology or occurrence date.

On initial examination, patient had an uncorrected visual acuity of 20/400 with no improvement with pinhole. Her pupil was noted to be slightly irregular with an equivocal relative afferent pupillary defect. Slit-lamp examination of the anterior chamber was unremarkable. On dilated fundoscopic examination, a large area of chorioretinal scarring was seen in the superior periphery with preretinal hemorrhage; the retina appeared attached without any obvious retinal tears or areas of gross neovascularization. A VH was present centrally causing poor visualization and discrimination of details of the major aspects of the posterior pole described above. A B-scan ultrasound was obtained with evidence of vitreous debris consistent with vitreous hemorrhage, but no retinal detachments or masses were detected. Color fundus photos were also obtained which confirmed the presence of the superior CR scar as well as a white retinal lesion along the inferotemporal

vascular arcade consistent with nerve fiber layer myelination (Figure 1). No scars or neovascularization were seen on dilated fundus examination or color fundus photos of the left eye.

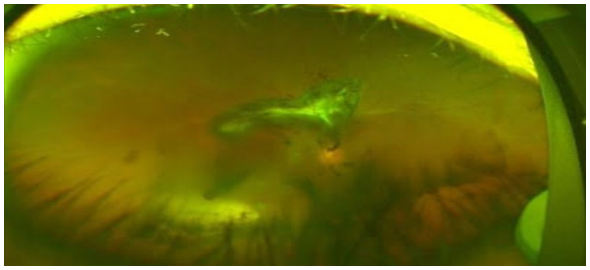

Figure 1: Color fundus photograph showing a chorioretinal (CR) scar in the superior peripheral retina along the super temporal vascular arcade, with a white lesion along the inferotemporal vascular arcade consistent with nerve fiber layer myelination (no active CR lesion). Notice the overlying vitreous hemorrhage that precludes the visualization of details of the posterior pole.

Patient was scheduled for a 25 plus gauge pars plana vitrectomy with possible membrane peel and endolaser, and underwent a pre-operative intravitreal injection of bevacizumab a few days prior to the surgery. A complete core vitrectomy with peripheral shaving was performed, effectively removing the VH. Endolaser was then used to surround the CR scar, without lasering the scar itself, as well as in 360 degrees of the peripheral retina for retinal detachment prophylaxis. Her VA improved to 20/50 on immediate post-operative follow up examination. Patient continued to do well with VA improving to 20/20 by the end of her post-operative follow up. Several months later (approximately 5 months), she endorsed new symptoms of the right eye consistent with pain, photophobia, redness, and a gradual blurring of vision over the few weeks prior to consultation. Slit lamp examination showed 3+ cells and flare in the anterior chamber, Koeppe nodules on the inner margin of the iris, and severe granulomatous keratic precipitates on the inferior corneal endothelium. Examination of the posterior segment showed 2+ vitreous haze and a new chorioretinal infiltrate nasal to the optic disc (Figure 2).

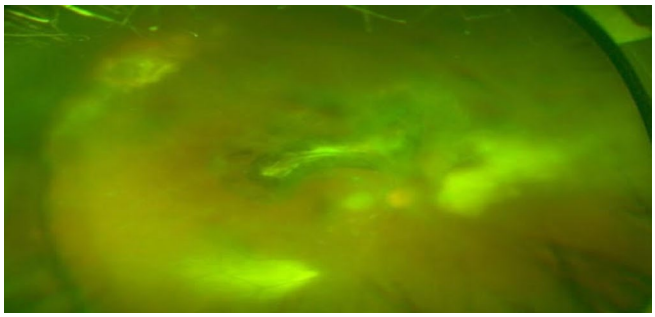

Figure 2: Color fundus photograph obtained on post-operative period depicting vitreous haze, a known inactive CR scar in the superior periphery along the superotemporal vascular arcade, and a new CR infiltrate nasal to the optic disc.

Our patient was diagnosed with panuveitis with a high suspicion for ocular toxoplasmosis given her racial background with a known previous chorioretinal scar of unknown etiology. A differential diagnosis was also considered including the causes for acute retinal necrosis from a viral infection. A vitreous tap was performed with samples sent to the laboratory for bacterial and fungal cultures, Gram stain, cytology evaluation, and Polymerase Chain Reaction (PCR) analysis for *Toxoplasma gondii*, Cytomegalovirus, varicella-zoster virus, and herpes simplex virus I & II. The PCR of the vitreous tap returned positive for Toxoplasma, with negative PCR results for the other agents. In addition, an enzyme-linked immunosorbent assay of a serum sample for anti-Toxoplasma antibodies showed high titers of immunoglobulin G, while serum immunoglobulin M (IgM) was absent. The IgM were not repeated due to the positivity of the PCR results obtained from the vitreous tap. The patient was treated with topical medications consistent with prednisolone acetate 1% and atropine 1% in addition to oral prednisone, and a combination of sulfamethoxazole and trimethoprim double strength (800 mg/160 mg) at standard doses for this ocular infection. This regimen was continued for several months until the ocular inflammation resolved and there was evidence of scarring of the CR infiltrate. By this time, her VA improved to 20/30 and the medications were slowly tapered off.

She continued to do well until a follow up exam a few months later revealed new subretinal and preretinal hemorrhage on dilated examination (Figure 3). The bleeding was localized to the area of the initial CR scar along the superotemporal vascular arcade. It was determined that the source of the new hemorrhage was from a reactivation of a CNVM associated with the initial VH from breaking through the vitreous cavity. The OPTOS wide-field imaging fluorescein angiography (OPTOS FA) (Figure 4) and spectral-domain ocular coherence tomography (SD-OCT) (Figure 5) confirmed the presence of an active CNVM associated with the CR scar, supporting the clinical diagnosis of a CNVM. In order to prevent further visual decompensation and the possibility of a new breakthrough with VH, the patient was treated with monthly intravitreal aflibercept over a six month course with successful resolution of the CNVM activity on serial OCT examinations.

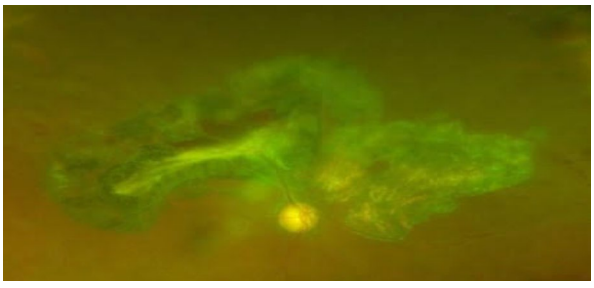

Figure 3: Color fundus photograph confirms bleeding (pre/subretinal hemorrhage) in area of superotemporal CR scar. Notice the area of CR scarring nasal to the optic disc consistent with the area of previous reactivation of ocular toxoplasmosis.

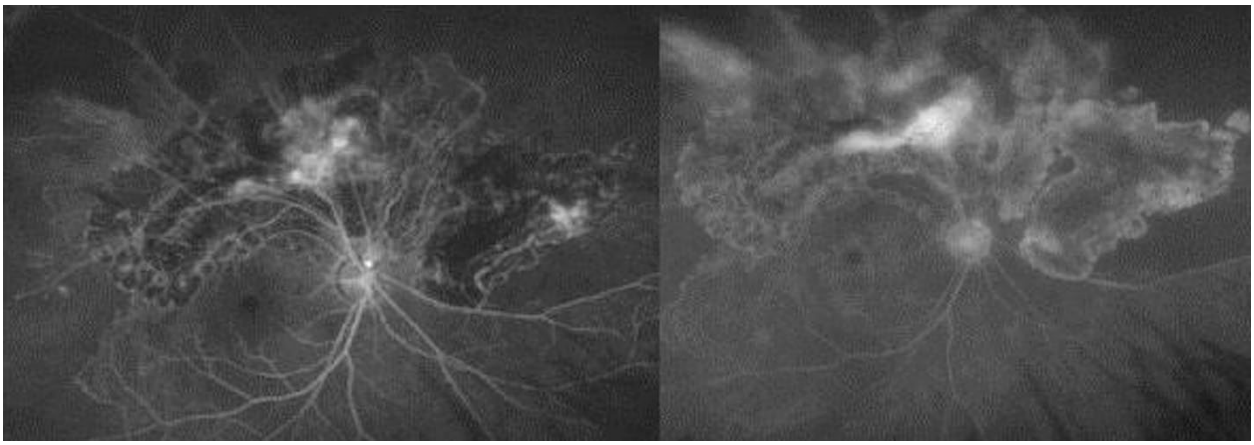

Figure 4: Early (left photo) and late (right photo) phase OPTOS FA confirming presence of an active CNVM with positive subretinal leakage from the supertemporal CR scar and blockage and staining from the nasal CR scar.

Discussion

In this case report we present an unusual case of CNVM that initially caused a VH. The VH was visually significant and required surgical removal with pars plana vitrectomy. The CNVM was a complication of a then revealed CR scar of unknown etiology following removal of VH. As the disease unfolded and the etiology of the CR scarring was clarified following reactivation of ocular toxoplasmosis, we were able to discern the behavior of the lesion. Finally, the patient developed in a more typical fashion with subretinal and preretinal hemorrhage and the corroboration of the CNVM with the aid of diagnostic imaging that allowed the more definitive treatment of the lesion.

CNV most commonly consists of an abnormal growth of vessels from the choroidal vasculature to the retina through Bruch's membrane [3]. While choroidal neovascularization is most commonly associated with the neovascular "wet" form of Age-related Macular Degeneration (AMD), it may also complicate a large spectrum of disorders that damage Bruch's membrane [4,5]. These include, but are not limited to, infectious inflammatory chorioretinopathies, such as the necrotizing chorioretinitis seen in ocular toxoplasmosis and presumed ocular histoplasmosis syndrome, non-infectious inflammatory chorioretinopathies, such as multifocal choroidal panuveitis and serpiginous choroidopathy, choroidal neoplasms, traumatic choroidal rupture, and optic disc abnormalities [5]. Regardless of the mechanism, there is clear evidence that once damaged, hypoxic retina produces Vascular Endothelial Growth Factor (VEGF), the main driver of retinal and choroidal neovascularization [6]. Neovascular disease in ocular toxoplasmosis is thought to be secondary to compromise of Bruch's membrane related to inflammation from active infection with T. gondii, as well as from increased expression of VEGF [7]. Prior studies on patients with CNV have even discovered autoantibodies against extracellular matrix proteins that compose the Bruch's membrane [4]. Damage to Bruch's membrane results in disruption of the normal transport of metabolites, ions, and water that nourish the Retinal Pigment Epithelium (RPE), leading to hypoxia and the eventual release of VEGF which triggers a cascade of angiogenic signaling at the level of the choroidal endothelium [3]. Injection of VEGF into the eye of a non-human primate stimulates growth and permeability of new vessels on the retina, simulating proliferative diabetic retinopathy, and also induces neovascular glaucoma [6]. Abnormal vessels cause exudation, hemorrhage, fibrosis and outer retinal degeneration, leading to symptoms of sudden onset decreased vision, metamorphopsia, and/or paracentral scotoma [5,8]. When a CNVM does develop, it has the potential to break through the vitreous cavity, resulting in formation of a VH which can also cause sudden onset decreased vision.

SD-OCT is the most efficient and reliable tool in both diagnosing CNV and monitoring its response to therapy [5]. There are three types of CNV currently recognized, each with distinguishing characteristics on SD-OCT [5]. Type 1 CNVM is when the membrane is located below the RPE, demonstrating an elevation of the RPE with a Pigment Epithelial Detachment (PED) [3,5] (Figure 5). This is often referred to as 'hidden' CNV. Type 2 CNVMs pass through the RPE and occupy the subneurosensory space above it; they appear as hyperreflective bands or plaques, with associated subretinal and/or intraretinal fluid [3,5]. Type 2 is known as 'classic' CNV. Finally, type 3 is defined as retinal angiomatous proliferation due to new blood vessels sprouting from the deep capillary plexus of the neurosensory retina, seen as a hyperreflective focus with or without associated CME and PED [3,5].

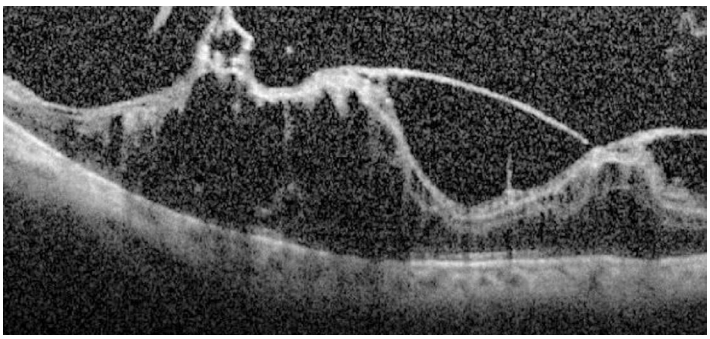

Figure 5: SD-OCT of the CR scar along the superotemporal vascular arcade. These findings demonstrate the massive cystoid thickening in relation to a CNVM.

There are different modalities of treatment for CNVM that have been utilized and explored over the past several decades. Many recent studies focusing on research of angiogenesis have shown that inhibition of VEGF with intravitreal anti-VEGF agents leads to the best results both histologically, with regression of the neovascular lesion, and functionally with improvement in VA [3,5]. The most effective preparations, bevacizumab (Avastin; Genentech Inc., South San Francisco, CA) or ranibizumab (Lucentis; Genentech Inc., South San Frnacisco, CA), are recombinant monoclonal antibodies (Fab) that neutralize all biologically active forms of VEGF [9]. More recently, aflibercept (Eylea; Regeneron Pharmaceutical Inc., Tarrytown, NY) a recombinant fusion protein that binds all forms of VEGF-A and PIGF proteins has similar actions. With continued anti-VEGF treatment, reproliferating CNV undergoes phenotypical maturation with distinctive vascular remodeling and concomitant decrease in leakage activity [10]. Significant research has been conducted regarding the utility of anti-VEGF given the prevalence of PDR with CNV in the developed world. The CLARITY (Clinical efficacy and mechanistic evaluation of aflibercept for proliferative diabetic retinopathy) study of 2015 showed that anti-VEGF therapy was superior to panretinal photocoagulation (PRP) in terms of improving BCVA in patients with PDR-this suggested that in addition to PRP, anti-VEGF should be used more widely as a conjunctive treatment for PDR to avoid complications such as VH or retinal detachments [11].

Prior to the advent of anti-VEGF therapy, Photodynamic Therapy (PDT) had been the first-line treatment for CNV. First introduced in 2000, PDT is still used in cases of CNV with polypoidal choroidal vasculopathy, recognized as a variant of type I CNV, and in cases refractory to and/or with tachyphylaxis to anti-VEGF drugs [9,12]. In a study comparing the response in treatment with either anti-VEGF or PDT for patients with CNV, the anti-VEGF group of drugs showed significantly better mean best corrected VA at each follow-up visit when compared with that of PDT, with superior efficacy sustained until 24 months after initial treatment [13].

Other treatment modalities that have been explored include translocation of the retina with surgical excision of subfoveal CNV, in which the fovea is moved to healthier RPE. Better outcomes were limited to patients with focal disorders of the RPE rather than those with diffuse disease [5,14], and surgical interventions have been abandoned over time due to poor visual outcome and complexities in comparison to pharmacologic interventions described above [5]. In more rare cases of CNVM associated with CR scars, such as in the case of our patient, CNVMs can break through the vitreous cavity, causing visually significant VH. In this case, a pars plana vitrectomy is a necessary treatment moadlity to improve visual outcomes. Future forms of therapy may soon be added to the arsenal of treatments at hand, to significantly inhibit leakage and growth of newly formed, as well as pre-existing CNV lesions [5,7,11,15].

In conclusion, CNV is a visually significant pathologic development that is seen in association with an extensive array of pathologic processes, affecting millions of people worldwide. In North America alone it is estimated that 200,000 new cases of neovascular AMD develop annually [5]. This only makes up a subset of the total number of patients who will be newly diagnosed with visually significant CNV. In order to provide the most effective care for patients, it is crucial to be able to recognize the different clinical presentations and histologic categorizations of CNV on SD-OCT. In addition, being knowledgeable of the many different treatment modalities currently available, with an awareness of possible future treatments being developed for patient care, can help limit complications and target the best treatment approach on an individual case basis.

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Author Contributions

A.D.: created the manuscript, performed literature review, and final edits of manuscript.

D.E.: retina specialist who followed the patient and performed surgical case management; co-writing of the manuscript, literature search, and manuscript editing and revision, as well as final approval.

References

1. Park YH, Nam HW (2013) Clinical features and treatment of ocular toxoplasmosis. Korean J Parasitol 51: 393-399.
2. Mushtaq F, Ahmad A, Qambar F, Ahmad A, Zehra N (2019) Primary Acquired Toxoplasma Retinochoroiditis: Choroidal Neovascular Membrane as an Early Complication 11: e4001.
3. Choroidal Neovascularization: OCT Angiography Findings (2019) Internet Material.
4. Nita M, Grzybowski A, Ascaso FJ, Huerva V (2014) Age-related macular degeneration in the aspect of chronic low-grade inflammation (pathophysiological parainflammation). Mediators of Inflammation. 930671.

5. American Academy of Ophthalmology (2017) Basic and Clinical Science Course 2017-2018: section 12: Retina and Vitreous. San Francisco.

6. Sivaprasad S, Prevost AT, Brainridge J, Edwards RT, Hopkins D, et al. (2015) Clinical efficacy and mechanistic evaluation of aflibercept for proliferative diabetic retinopathy (acronym CLARITY): a multicenter phase IIb randomised active-controlled clinical trial BMJ Open 5: e008405.

7. Benevento JD, Jager RD, Noble AG, Latkany P, Mieler WF, et al. (2008) Toxoplasmosis-associated neovascular lesions treated successfully with ranibizumab and antiparasitic therapy. Arch Ophthalmol 126: 1152-1156.

8. Yang JY, Madrakhimov SB, Ahn DH, Chang HS, Jung SJ, et al. (2019) mTORC1 and mTORC2 are Differently Engaged in the Development of Laser-Induced CNV. Cell Communication and Signaling 17 (1).

9. Regatieri CV, Branchini L, Duker JS (2011) The role of spectral-domain OCT in the diagnosis and management of neovascular age-related macular degeneration. Ophthalmic Surg Lasers Imaging 42: S56-S66.

10. Faes L, Ali Z, Wagner S, Patel PJ, Fu DJ, et al. (2019) Effect of total anti-VEGF treatment exposure on patterns of choroidal neovascularisation assessed by optical coherence tomography angiography in age-related macular degeneration: a retrospective case series. BMJ Open Ophthalmol 4: e000244.

11. Wirkkala J, Bloigu R, Hautala NM (2019) Intravitreal bevacizumab improves the clearance of vitreous haemorrhage and visual outcomes in patients with proliferative diabetic retinopathy. BMJ Open Ophthalmol 4: e000390.

12. Sayanagi K, Hara C, Fukushima Y, Sato S, Sakaguchi H, et al. (2019) Time course of swept-source optical coherence tomography angiography findings after photodynamic therapy and aflibercept in eyes with age-related macular degeneration. American Journal of Ophthalmology 15: 100485.

13. Kang HM, Koh HJ (2013) Intravitreal Anti-Vascular Endothelial Growth Factor Therapy Versus Photodynamic Therapy for Idiopathic Choroidal Neovascularization. American Journal of Ophthalmology 155: 713-719.

14. Thomas MA, Dickinson JD, Melberg NS, Ibanez HE, Dhaliwal RS (1994) Visual Results after Surgical Removal of Subfoveal Choroidal Neovascular Membranes. Ophthalmology 101: 1384-1396.

15. Livnat T, Weinberger Y, Budnik I, Deitch I, Dahbash M, et al. (2019) Activated Protein C Induces Suppression and Regression of Choroidal Neovascularization-A Murine Model. Experimental Eye Research 186: 107695.