A 53-Year-Old Female with a Retinal Hemorrhage

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Introduction:

A 53-year-old white female was referred to The Retina Institute for evaluation of a macular hemorrhage in her left eye. The patient described a sudden onset of painless vision loss that occurred about 2 weeks prior to our visit. Her past ocular history was only remarkable for astigmatism, and she reported that she was having difficulty adjusting to her new glasses prescription in both eyes over the past several months. Her medical history was significant for hypertension. A review of systems was unremarkable.

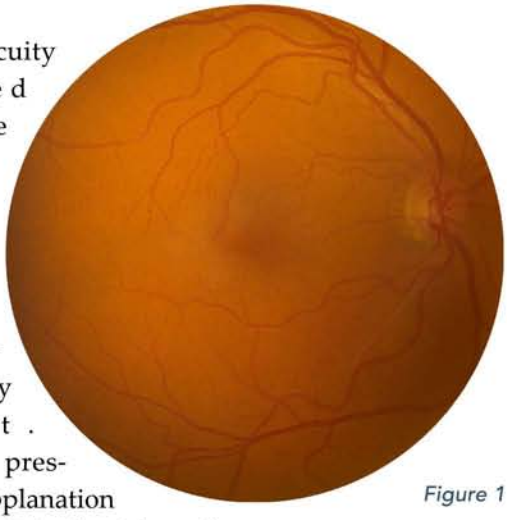


Figure 1

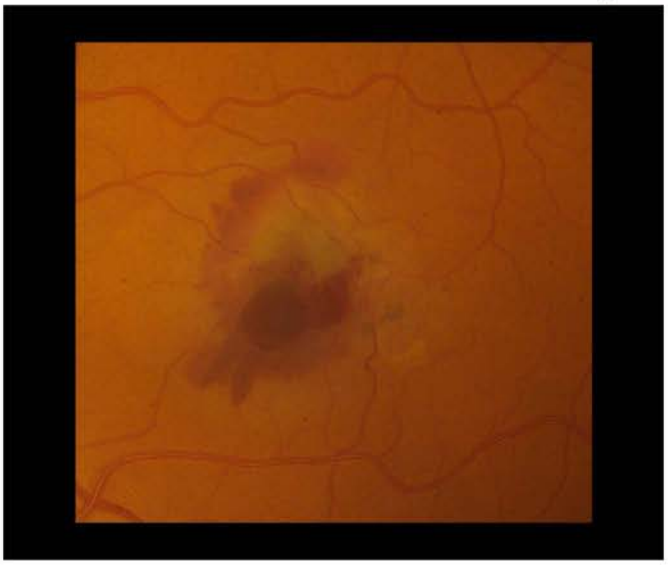
Visual acuity measured 20/40 in the right eye and 5/200 in the left eye. There was no relative afferent pupillary defect. Intraocular pressures by applanation were 23 and 15 in the right and left eyes, respectively. Anterior segment examination showed mild nuclear sclerosis in both eyes.

Dilated fundus examination showed vitreous syneresis in both eyes, and the optic nerves were sharp and pink. The macula in the right eye was clinically dry with a good foveal light reflex (Figure 1), but the left macula showed intra- and sub-retinal hemorrhage with an adjacent neovascular complex (Figure 2, 3). The vessels and periphery were otherwise unremarkable in both eyes.

At this point optical coherence tomography (OCT) and fluorescein angiogram were obtained to better characterize the macular lesion in the left eye. OCT of the right eye revealed a hyporeflective cavity along the temporal slope of the foveal pit (Figure 4). There was also loss of the photoreceptor inner segment/outer segment (IS/OS or ellipsoid zone) layer temporal to the foveal center. Fluorescein angiography of the right eye

Figure 2

Figure 3



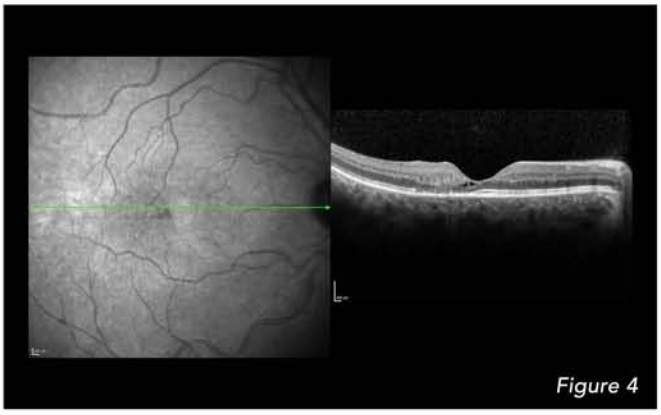
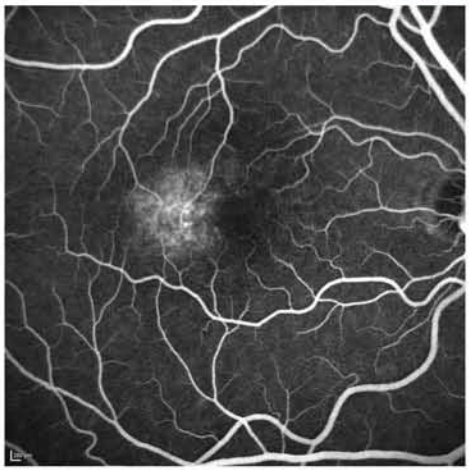


Figure 4

showed telangiectatic vessels temporal to the fovea and diffuse late staining in the temporal foveola (Figure 5).

In the left eye, the OCT showed a neovascular complex within the retinal layers in addition to intra- and sub-retinal fluid and hemorrhage (Figure 6). Corresponding angiogram of the left eye revealed diffuse blockage of fluorescein due to hemorrhage in addition to telangiectatic vessels and late leakage in the temporal foveola (Figure 7).

Figure 5



Based on the patient's clinical, angiographic, and tomographic findings, we diagnosed her with macular telangiectasia (MacTel) type 2. To limit the activity of the neovascular complex, she was treated in our office with intravitreal bevacizumab in the left eye.

Discussion:

The differential diagnosis for MacTel type 2 includes exudative macular degeneration (AMD), bilateral branch retinal vein occlusions, hypertensive retinopathy, diabetic retinopathy, ruptured retinal arterial macroaneurysm, and radiation retinopathy. Other less common conditions on the differential include MacTel type 1 (although it would not be bilateral), Sjogren-Larsson syndrome, Eales disease, and solar retinopathy.

MacTel type 2 was first reported by Donald Gass in 1977 as "bilateral paracentral capillary telangiectasia of unknown cause"[1]. Affected patients have characteristic alterations of the capillary network in the macula and progressive atrophy in the neurosensory retina involving the foveal center[2]. Patients usually present with visual symptoms in the fifth to sixth decade, and some may have a positive family history. The diagnosis of MacTel type 2 is often delayed due to low disease awareness amongst clinicians, and in the presence of CNVM or macular hemorrhage, it is often misdiagnosed as exudative age-related macular degeneration.

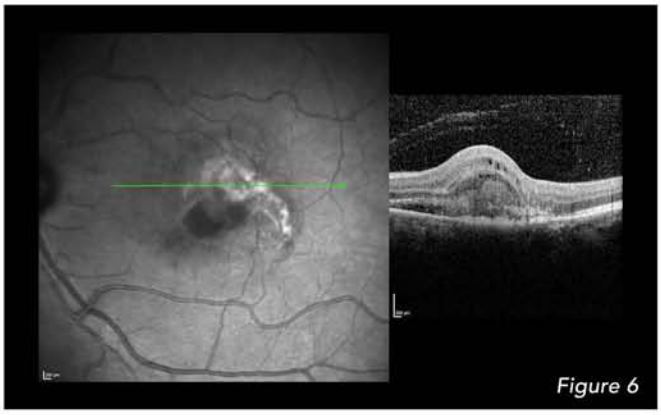


Figure 6

The NIH- sponsored Macular Telangiectasia Project ("MacTel Project"; www.mactelresearch.org) was initiated in 2005 in an effort to better understand the pathogenesis, clinical features, natural history, and genetic association of MacTel type 2 with the ultimate goal of identifying and testing possible treatments for this little-known disease. Seventeen pedigrees with multiple affected members have been identified thus far, suggesting a dominant inheritance with reduced penetrance and variable phenotypic expressivity[2]. However, efforts to identify a genetic defect responsible for MacTel type 2 have been unsuccessful.

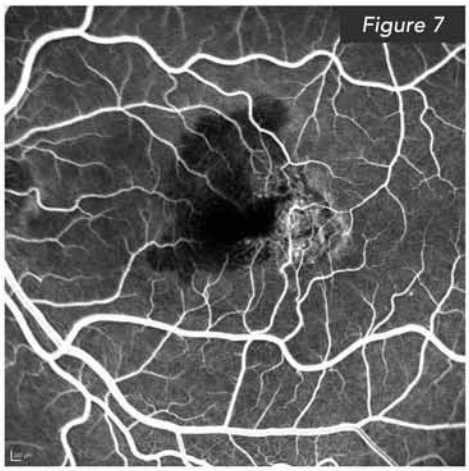


Figure 7

Clinical Findings:

Funduscopic findings may be very subtle n MacTel type 2, particularly in the early stages of the

disease, one eye may be more affected than the other, as demonstrated in our patient's case. Retinal alterations usually begin in the temporal paracentral macula. Despite a normal appearing fundus, the earliest manifestation of MacTel type 2 can be appreciated as diffuse hyperfluorescence in the late phase of fluorescein angiography. On OCT, inner and outer retinal defects are seen most commonly in the temporal macula, and these hyporeflective cavities are often mistaken for cystoid macular edema (CME) or lamellar macular holes. Unlike other causes of CME (i.e. diabetes, pseudophakic CME, etc.), these hyporeflective spaces do not leak or pool fluorescein dye on angiography[3]. Progression of the disease then leads to loss of retinal transparency, followed by the appearance of dilated right angled venules and crystalline parafoveal deposits. In the later stages, foveal atrophy and loss of the IS/OS (ellipsoid zone) can be seen on OCT. Prolonged atrophy of the photoreceptor layer inevitably leads to retinal pigment epithelium (RPE) hyperplasia and intraretinal pigment clumping.

Complications from this disease include true lamellar or full thickness macular holes and neovascular complexes that cause retinal edema, exudates, and intra/subretinal hemorrhage. Unlike the CNVMs that develop from exudative AMD, the neovascular complexes in MacTel type 2 appear to be retinal in origin, and they gain access to the subretinal space by developing chorio-retinal shunts[4]. These neovascular complexes can develop at any stage during the disease.

Despite an average visual acuity of 20/40 in the 522 untreated eyes of the MacTel Project cohort, the majority of patients had some form of metamorphopsia on amsler grid testing, and there was a significant degree of decreased reading ability (both reading speed and acuity) due to a paracentral absolute scotoma2. Therefore, using distance visual acuity alone as a measure of a patient's visual function may belie the true underlying impact this disease may have on a patient's quality of life.

Treatment:

A number of approaches have been reported for the treatment of MacTel type 2 including focal argon laser, photodynamic therapy, intravitreal triamcinolone, and intravitreal anti-VEGF agents. Due to the rare nature of this disease, most reports are single cases or small retrospective case series. The slow progression of the disease makes it difficult to measure treatment effects, as outcomes of these small case studies are usuallymeasured over a short period of time. For patients with theproliferative stage of the disease (i.e. development of a neovascular complex), several studies have demonstrated that intravitreal anti-VEGF treatment is beneficial in stabilizing visual acuity and limiting the activity of the neovascular complex[2]. However, since the natural course of this disease is slowly progressive photoreceptor loss and foveal atrophy, there has been no proven treatment in MacTel type 2 patients without proliferation. A phase 2 multicenter randomized clinical trial is currently underway to study the use of ciliary neurotrophic factor (CTNF) as a potential treatment for MacTel type 2[2].

Conclusion:

This case illustrates how "older" ancillary tests such as fluorescein angiography are still important for characterizing diseases that would be missed on routine fundus examination (i.e. the FA findings in the right eye helped clinch the diagnosis of MacTel 2 as the cause of this patient's submacular hemorrhage). Our patient did well after one injection of intravitreal bevacizumab and her visual acuity improved to 20/100 in the left eye at the one month follow-up visit. We will be monitoring her closely for continued resolution of her retinal edema and subretinal hemorrhage.
Since it was first described by Dr. Gass in 1977, little else has been elucidated about macular telangiectasia type 2 until recently. Although there is still much progress to be made in understanding this neurodegenerative disease, the recent Macular Telangiectasia Project is a promising step in the right direction towards finding an effective treatment for the non-proliferative form of this disease.

References:

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