Chorioretinal Folds: Associated Disorders and a Related Maculopathy

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Purpose: To describe a series of chorioretinal folds represent a clinical sign that may be associated with multiple systemic, orbital and ophthalmologic disorders. We report both the associations with systemic disease and describe three stages of a chorioretinal fold-related maculopathy.

Design: Observational, retrospective case series.

Methods: We reviewed fifty-seven affected eyes from 40 patients with the clinical sign of CRF from one of two academic institutions. A careful review of the medical histories and systemic diagnostic evaluations were conducted. Imaging studies were conducted.

Results: The mean age at diagnosis was 64 ± 17 years. Most eyes (18) were hyperopic (+2.60 ± +2.90 diopters). There were 20 patients (50%) with some form of autoimmune disorder. Overall, the mean presenting visual acuity was 20/50, declining slightly to 20/60 over 19 ± 30 months. Ten eyes had stage 3 CRF related maculopathy, more common in older individuals with more chronic CRFs. Four stage 3 eyes had associated choroidal neovascularization (CNV) and these eyes presented with 20/60 visual acuity and dropped to 20/100 over approximately 1.5 years. Stage 3 eyes without CNV, had a mean presenting visual acuity of 20/40 and decreased to 20/65 over 2.1 years.

Conclusions: Chorioretinal folds are associated with numerous ophthalmic and systemic disorders. A careful medical history and evaluation is essential. We describe three stages of a unique chorioretinal fold-related maculopathy. Stage 3 resembles occult CNV, occurs primarily in older individuals with chronic chorioretinal folds and is accompanied by a slow deterioration in central acuity.
Chorioretinal Folds:
Associated Disorders and a Related Maculopathy

Short Title: Chorioretinal Folds, Associated disorders and Maculopathy

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Introduction:

Chorioretinal folds were first described in 1884 by Nettleship in a patient with papilledema.\(^1\) Birch-Hirschfeld and Siegfried demonstrated with histopathology that the folds extended into the neurosensory retina.\(^2\) Chorioretinal folds represent a relatively uncommon clinical sign that should prompt the clinician to consider numerous potential etiologies, ranging from minor hyperopia to serious systemic disorders such as neoplastic, infectious, or immunologic disorders.

In the 1950’s, the suspicion of systemic disease associations with chorioretinal folds was heightened and chorioretinal folds were considered to represent an ominous sign. By 1959 and 1962 respectively, Hedges\(^3\) and then Wolter\(^4\) pointed out that chorioretinal folds could be the presenting sign of an orbital tumor indenting the sclera. Over time, clinicians have become more adept at diagnosing and detecting chorioretinal folds during fundoscopic examination and have associated this important clinical sign with ocular, orbital, and systemic conditions. An important, and some may argue obvious clarification, is that chorioretinal folds represent a clinical sign, rather than a specific diagnosis.

The disease-related categories associated with chorioretinal folds include inflammatory, neoplastic, infiltrative, and infectious. The list of specific diagnoses that have been associated with chorioretinal folds has increased along with improvements in our diagnostic capabilities, thereby, leaving the exclusionary category of idiopathic chorioretinal folds decreasing proportionately. Common diagnoses that have been associated with chorioretinal folds include thyroid eye disease,\(^5\) posterior scleritis,\(^6,7\) tumors,\(^3,8\) hypotony,\(^9\) the uveal effusion syndrome,\(^10\) hyperopia,\(^11\) post-scleral buckling surgery,\(^12\) and age-related macular degeneration (AMD).\(^7,13,14\) There is sufficient evidence that once the clinician recognizes the presence of chorioretinal folds as a clinical sign, a prompt systemic investigation for a specific diagnosis or etiology is mandatory.

Anatomically, chorioretinal folds represent undulations of the inner choroid, Bruch's membrane, overlying retinal pigment epithelium (RPE), as well as secondarily affecting the overlying neurosensory retina.\(^14\) In 1972, Newell proposed that chorioretinal folds developed as a result of the strong connection between Bruch’s membrane and the underlying choriocapillaris. As the choroid swells or expands, the overlying Bruch’s membrane is forced into folds, thus leading to the clinical appearance of chorioretinal folds.\(^15\) Friberg elegantly provided a biomechanical analysis that further explained the evolution of chorioretinal folds. He proposed that chorioretinal folds develop as a result of the stress and strain relationship that occurs between the sclera and choroid, with a reduction in the area of the inner lining of the sclera, resulting in a buckling force affecting the choroid from either scleral thickening or shrinkage. Furthermore, Friberg suggested that chorioretinal folds represent a potential risk factor for RPE atrophy and potentially irreversible injury to Bruch’s membrane, leading to an angiographic appearance that resembles angiod streaks.\(^12\)
Herein, we present a series of patients with the clinical sign of chorioretinal folds that have been reviewed from two tertiary academic centers (the University of Minnesota and Emory University). The associated systemic and ophthalmologic diagnoses represent broad ranging etiologies that may contribute to the formation of chorioretinal folds. Furthermore, we describe a specific maculopathy (chorioretinal folds maculopathy) that evolves in selected cases of chronic chorioretinal folds, especially in older patients.

Methods:

The institutional review board of the University of Minnesota and Emory University approved the retrospective review of patient data for this study. We reviewed the medical records of consecutive patients with the clinical sign of chorioretinal folds. Forty patients were identified with the clinical sign from either the medical record database or by searching the fundus photographic imaging database. Demographic information including age at presentation, ocular and medical history, duration of follow-up, potential etiologies, or associated diagnoses (either systemic, ophthalmologic, or both) were recorded for each patient. The best corrected Snellen visual acuity, fundoscopic features, refraction and axial length (when available), clinical diagnosis requested with the imaging studies (fundus photography, ocular coherence tomography, fluorescein angiography), and specific treatment modalities were also noted. All statistical analysis was performed using a paired Student's t-test. Statistical significance was defined as P<0.05.

Results:

Fifty-seven eyes of 40 patients were identified with a history of chorioretinal folds. Seventeen were bilateral while 23 were unilateral. The mean age at presentation was 64 years ± 17 (± SD; standard deviation) with ages ranging from 27 to 96. Other demographics collected are listed in Table 1. Nineteen (48%) had a history of hypertension (although the presence of hypertension was not documented in 21 of our records) and 11 (28%) had a history of autoimmune disease. Eighteen of those in whom a refraction was documented were hyperopic with a mean refraction of +2.4 diopters. Eleven (28%) had clinical features of age-related macular degeneration. The mean follow-up was 19 ± 30 months (range 0-156 months).

Selected chorioretinal folds should be considered secondary chorioretinal folds and are related to a specific abnormality located at the chorioretinal interface such as a scar/fibrosis or choroidal neovascular complex (Figure 1). Six eyes were identified as having secondary folds that resulted from scarring or fibrosis related to exudative AMD (4), from other chorioretinal scarring (1), or from a scleral buckle (1).
Primary chorioretinal folds involve pathologies that affect the choroid or sclera directly and are typically are arranged as linear or parallel folds that generally extended directly through the central macula. In 19 eyes, the chorioretinal folds projected mostly along the temporal arcades, or less commonly radiated from the optic nerve (5 eyes). Others had varying and more random distribution of chorioretinal folds (8 eyes). A significant portion of eyes (n=14) developed a pigmentary maculopathy (Figure 2). Two patients had a submacular hemorrhage, presumably from a rupture of Bruchs in membrane that resulted directly from the folds that were not clearly associated with angiogenesis or neovascularization.

Multiple conditions or diagnoses were associated with the chorioretinal folds. Cases identified in our series as listed in decreasing frequency include (note that there is overlap): hypertension (19), hyperopia (18), idiopathic/unidentified (6), age-related macular degeneration (secondary chorioretinal folds; n= 11), autoimmune disease (11), rheumatoid arthritis (5), uveal effusion syndrome (4), posterior scleritis (4), hypotony (3), thyroid eye disease (3), choroidal infiltrates (i.e. lymphoma) (2), orbital mass (2), inflammatory bowel disease (3), and several isolated associations that included vitiligo, polymyalgia rheumatic, systemic lupus erythematosis, Lyme disease, psoriasis, multiple sclerosis, and ethmoid sinusitis (Table 1). Overall, nearly half (20 of the 40 patients) had some form of autoimmune disorder. Note that some had overlapping conditions such as rheumatoid arthritis and scleritis. Twelve of our patients were pseudophakic at time of presentation, and information about their specific refractive state prior to surgery was not available. Therefore, it is possible that some patients in the idiopathic group may represent additional cases with hyperopia.

Excluding patients with secondary chorioretinal folds, a comparison of the visual acuity at the initial visit to the latest follow-up visit (mean 19 ± 30 months) demonstrated a decline of one line of Snellen acuity (20/50 to 20/60; respectively, p=0.01). Therefore, a decline in best-corrected visual acuity is a slow process in primary chorioretinal folds.

Fluorescein angiography was available for 22 patients. Three progressive angiographic stages were observed: First, in stage 1, there are alternating bands of hyper- and hypofluorescence characteristic of choroidal folds (n=8; Figure 3). Next, in stage 2, there are beginning to form areas of staining that correspond to early breakdown of the retinal pigment epithelium along with breaks in Bruch’s membrane (n=6; Figure 2). And finally, in stage 3, the chorioretinal fold related maculopathy is best exemplified in figures 4 and 5. In the more advanced stage three, the clinical appearance is usually associated with either a yellow, luteal macular appearance or atrophy of the RPE; plus, there are more prominent areas of RPE hyperplasia. On fluorescein angiography, the early phase has a stippled pattern of hypofluorescence (n=8) while in the later frames of the angiogram, there is increasing stippled hyperfluorescence with both staining and mild leakage. This pattern has also been described in occult choroidal
neovascularization (CNV) referred to as _late leakage of undetermined source_ by the Macular Photocoagulation Study (MPS) (Figure 4 and 5).  

Ten eyes of eight patients had stage 3 macular changes. The mean age of this group was 68 years, as compared to stage 1 (56 years; p<0.01) and stage 2 (64 years; p=0.2), respectively. In stage 3, the mean Snellen visual acuity was 20/60 at initial visit and 20/100 at the latest follow-up visit. Half of the stage 3 patients had chorioretinal folds extending through the center of the macula while the remainder had folds along the temporal arcades. The etiology of the more chronic chorioretinal folds with stage 3 chorioretinal folds-related maculopathy included rheumatoid arthritis, posterior scleritis, and hyperopia (usually > 3 diopters).

Six eyes of 4 patients with stage 3 maculopathy did not require anti-CNV therapy. In this group, the initial visual acuity was 20/40 and the final visual acuity was 20/65 at 25 months average follow-up (p=0.06). This data suggests that this group has a poor prognosis with gradual loss in central acuity once at stage 3. Four stage 3 eyes were suspected to have active CNV and were treated. Three of the four did not have evidence of CNV at presentation. Two of the four had small subretinal hemorrhages at or near the fovea. In the treatment group, mean visual acuity at the initial visit was 20/80, yet it decreased to 20/160 at 19 months average follow-up. Statistical analysis did not reach a level of significance because the number in this group was too small. None of the eyes that were treated had a measurable improvement in visual acuity.

Of those treated in stage 3, two patients received a periocular corticosteroid injection without an improvement in macular status or central visual acuity. One patient, managed in the pre- anti-VEGF era, was treated with submacular surgery and experienced a recurrence or persistence of the CNV within one month of surgery. Photodynamic therapy was then performed to successfully treat the recurrent CNV. Nevertheless, the visual acuity failed to improve. In the other three stage 3 eyes, the treatments performed did not result in a significant improvement in the central visual acuity or in the angiographic appearance. During the anti-VEGF era, a single intravitreal bevacizumab was administered in one stage 3 eye with active leakage and after a failed periocular corticosteroid injection. The angiogram performed one month after injection demonstrated a clear resolution of the leakage pattern and the eye did not require further therapy. However, there was no improvement in visual acuity. Separately, an intravitreal ranibizumab was administered to a patient with stage 3 and a possible CNV that also had an accompanying subretinal hemorrhage. This lesion also regressed after a single injection and did not recur during a 22-month follow-up interval. There were no changes in visual acuity (see case 1 below; Figure 7).
Case 1:

A 63-year-old male presented with a paracentral scotoma in his right eye for 5 days duration. Chorioretinal folds were noted in the macula. Just nasal to the fovea, there was a small subretinal hemorrhage. An OCT showed undulations of the RPE consistent with chorioretinal folds as well as a subtle elevation of the RPE with surrounding subretinal fluid (Figure 6). The patient was treated with a single intravitreal injection of ranibizumab. On follow-up examinations the vision remained 20/20 and SD-OCT showed resolution of his subretinal process. Over a 22-month follow-up period, there was no recurrence.

Case 2:

A 75-year-old Caucasian male hyperopia had a long-standing decreased central visual acuity in his left eye after cataract surgery. The visual acuity was 20/20 in the right eye and 20/400 from the left. Chorioretinal folds were present along with pigmentary changes in the fovea and a prominent luteal appearance in the left macula. No subretinal fluid was noted on examination and confirmed by OCT. Three months later, visual acuity decreased to counting fingers at 2 feet in the left eye. A sub-Tenon’s injection of 40mg of triamcinolone was given with no improvement. FA demonstrated prominent chorioretinal folds with stippled hyperfluorescence in the macula and late leakage (Figure 4) while the OCT demonstrated mild subretinal fluid. An intravitreal bevacizumab injection was given. One month later, repeat FA showed no leakage yet there was no improvement in visual acuity.

Discussion:

We present 40 patients with 57 eyes and the uncommon clinical sign of chorioretinal folds. Similar to other series, we found that the majority of chorioretinal folds were secondary to structural changes of the globe. Chorioretinal folds represent a unique clinical sign that warrants a careful search for systemic or associated disease states. Table 1 lists the more common associations in our case series and strongly suggests that a careful clinical history along with systemic testing is necessary and may lead to the recognition and diagnosis of an autoimmune, inflammatory disorder, or neoplastic disorder.

Chronic chorioretinal folds involving the macula, may result in a unique chorioretinal folds-related maculopathy. In this condition, the tissues and visual function have a specific angiographic appearance that leads to an insidious progression and gradual decline in visual acuity over time. We've described chorioretinal folds-related maculopathy in three stages with degenerative macular features seen primarily in later stage 3 eyes. The angiographic features resemble the occult CNV described in AMD, referred to as late leakage of undetermined source. However, the chorioretinal folds-related maculopathy is...
progressive and the occasional CNV that may result seems to respond to very infrequent anti-VEGF injections.

Local orbital pathologies should always be carefully considered. Specifically, a flattened or thickened posterior sclera that may be detected on MRI imaging or B-scan ultrasonography is also associated with chorioretinal folds. Etiologies for this finding may range from hyperopia (most benign), posterior scleritis, to orbital tumors. On the other hand, secondary chorioretinal folds form from fibrosis or scarring within the chorioretinal interface, such as in involutional exudative AMD. While secondary chorioretinal folds are usually the result of scarring or fibrosis, clearly, there may be an associated significant decline in visual acuity. The suspicion for systemic disease is lower in these cases.

In the literature, two large case-series of chorioretinal folds have been published. Cangemi et al. published a series of 59 eyes with chorioretinal folds and found that the most common associated condition was hyperopia while 17% were idiopathic. Leahey et al. published a series of 78 eyes of 54 patients with the clinical sign of chorioretinal folds. In this series, the most common cause of folds was AMD, hyperopia, and idiopathic.

We propose that with improved diagnostic testing, the patients, formerly referred to as idiopathic, continue to represent a smaller portion of the total. In our study of 40 patients, six (15%) were considered to be idiopathic. Friberg proposed that such eyes may have had prior episodes of posterior scleritis, thus leading to permanent thickening of the posterior sclera and flattening of the posterior globe. Of our six patients with idiopathic folds, five had a history of autoimmune disease including rheumatoid arthritis, systemic lupus erythematosus, and Crohn’s disease. Therefore, it is quite plausible that a previous episode of undiagnosed ocular inflammation may have occurred that then led to the formation of chorioretinal folds.

Chorioretinal folds have been proposed to develop as the result of tractional forces emanating from the optic nerve. More recently, folds are believed to result from “. . . any intra- or extracocular process that induces sufficient compressive stress within the choroid, Bruch’s membrane, and retina to force these tissues to buckle.” Folds may occur secondary to any process causing choroidal swelling such as an effusion or infiltration, shrinking of the inner sclera (posterior scleritis), or a specific mechanical deformation. The difference in surface area between the two layers creates tension and stress on Bruch’s membrane with subsequent chorioretinal folds formation. As Friberg has demonstrated, the greater elasticity of the choroid compared with the sclera explains why the choroid folds and the sclera flattens. Secondary folds may form due to abnormal adhesions within the chorioretinal interface. Chorioretinal scars and subretinal neovascularization may lead to fibrosis, contraction, and secondary tractional influences on the surrounding retina and choroid producing radial chorioretinal folds (Figure 1).
For each etiology of chorioretinal folds, the anatomic and pathophysiologic response has a final common pathway that may either resolve acutely or develop into any of the three stages of chorioretinal folds-related maculopathy. Diagnostic imaging modalities such as color fundus photography, enhanced depth OCT, FA, or indocyanine green angiography (ICG) may help to characterize the pathologic and anatomic changes occurring in the choroid, Bruchs membrane, and RPE layers.

Haruyama et al. previously described the appearance of ICG angiography in patients with chorioretinal folds. The authors show delayed filling in choroidal vessels during the early transit phase followed by choroidal venous dilation (Figure 6), suggesting choroidal vascular congestion. Vascular congestion of the choroid may result from resistance of choroidal outflow that may result from extravascular interstitial edema that accompanies many inflammatory conditions. Additionally, there may be structural alterations within the scleral wall that may impair inflow through the short posterior ciliary arteries or outflow through the vortex ampulae. Poor venous outflow, delayed choroidal filling, and interstitial edema may result in an ischemic choroidal environment. Logically, similar abnormalities are not seen in patients with secondary radial folds.

Over time, Gass suggests that there are regions of high tensile stress that form along the convex surface and valleys of the chorioretinal folds. Clearly, there is a linear relationship between aging and the loss of elasticity in Bruchs membrane-choroid complex. As Bruchs membrane ages, the structure becomes thickened and calcified. The accompanying increase in fragility of Bruch’s along with the mechanical stress created by the folds will predispose Bruchs to fracture in the macular region especially in an aged eye. A fractured Bruchs in a relatively ischemic environment creates an ideal situation for formation of CNV. Interestingly, in this series, we found relatively few cases of CNV associated with chorioretinal folds. Four of our 40 patients (10%) developed CNV. Of the stage 3 chorioretinal folds-related maculopathy eyes, we found 4 of 10 (40%) developed evidence of CNV. Therefore, later stages should be monitored more closely for signs and symptoms related to the new onset of CNV. While some of the CNV cases occurred prior to the anti-VEGF era, our limited experience suggests that fewer injections are required than one would suspect in the management of CNV associated with AMD. Of those that were treated, none showed improvement in visual acuity while 2 had a decrease in acuity. One patient was treated with intravitreal bevacizumab for an extrafoveal CNV and had an improvement in angiographic leakage, yet no improvement in visual acuity. Another received a single intravitreal ranibizumab with resolution of both subretinal hemorrhage and fluid. Given that the acuity loss was more severe in the treatment group as compared with the observation group, chorioretinal folds related maculopathy does not seem to warrant aggressive treatment.

Fluorescein angiography has been extremely helpful in highlighting and identifying chorioretinal folds as well as to characterize the chorioretinal folds related maculopathy. Norton highlighted the alternating pattern of hyper and
hypofluorescence that corresponds to the crests and valleys of the chorioretinal folds, respectively. Gass later attributed this pattern to a greater volume of fluorescein in the folded, thicker choroid, a shorter course traveled by the reflected light at the apex with thinner RPE, and the clustered or redundant RPE within the valleys that blocks fluorescence. Macular pathology secondary to chronic folds was first reported by Newell, who noted cases of RPE pigment clumping and atrophy as well as linear streaks of fluorescein staining along the folds. Friberg and Grove presented two cases of subretinal neovascularization in the setting of chorioretinal folds. In their cases, fluorescein angiography demonstrated late hyperfluorescence corresponding specifically to a small choroidal neovascular complex. They also proposed that the loss of elasticity in Bruchs membrane combined with local stresses from chorioretinal folds could precipitate breaks and subsequent subretinal neovascularization.

The similarities of chorioretinal folds-related maculopathy to occult forms of CNV detected in AMD is remarkable. Late leakage of undetermined source as defined in the Macular Photocoagulation Study (MPS) has a unique fluorescence pattern with early hypofluorescence or delayed filling followed by late, poorly demarcated leaking hyperfluorescence (usually around 2 minutes) in the later phases of the angiogram. We have demonstrated a very similar FA pattern in cases of chorioretinal folds that may result from a mechanical injury and relative ischemia at Bruchs membrane (Figures 4 and 5). Clearly, not all chorioretinal folds result in this form of maculopathy, yet stage 3 chorioretinal folds-related maculopathy may be more commonly found in an aged Bruchs membrane with choroidal ischemia. While leakage may represent the vascular incompetence (thus leakage) of a damaged Bruchs membrane, one should be careful to assess for subretinal fluid and suspect CNV. We suggest OCT as a recommended complimentary imaging technique to standard angiography.

In the patients identified to have angiographic leakage not associated with CNV, we noted a trend towards declining central visual acuity. Most patients in our series were not treated; however, many presented prior to the anti-VEGF era. While the risks associated with the use of intravitreal anti-VEGF therapy is low, treatment may not be necessary, as the majority of acuity loss in our series seems to result from degenerative changes to the RPE-Bruchs complex. Even though the clinical and angiographic patterns resemble occult CNV, we suggest that a period of careful observation, imaging and monitoring is warranted.

There are several limitations to the current study. First, our study is retrospective. Current technology and therapeutic options were not available over the time period for collection of these less common cases. There are inconsistent follow-up visits so a careful comparison or outcome analysis is extremely difficult. Nevertheless, there may also be some significant advantages to examining these patients prior to the current aggressive use of anti-VEGF agents. Because our patients were studied before current pharmacotherapies, we were better able to study the natural course of CFR-related maculopathy.
In summary, we describe a large series of patients with chorioretinal folds that were carefully evaluated to detect potential systemic or orbital disease processes. The clinician needs to be acutely aware of the many systemic associations with this important clinical sign. The patient requires a careful medical history and examination for inflammatory, neoplastic, infectious, and infiltrative disorders. A high percentage of our cases had associated inflammatory systemic conditions. Furthermore, we would also like to describe the three stages of chorioretinal folds-related maculopathy. This unique maculopathy has been confused with occult choroidal neovascularization. The angiographic pattern of this maculopathy resembles late leakage of undetermined source as defined by the MPS, and is more commonly seen in stage 3 chorioretinal folds-related maculopathy, especially in older individuals. This unique maculopathy has a slow and indolent course with gradual macular dysfunction that evolves over many years. The judicious use of anti-VEGF therapy should be considered when there is OCT evidence of subretinal fluid.
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b. Financial Disclosures: none

c. Contribution of Authors:
   a. Design of Study: NP, TO
   b. Conduct of Study: NP, SY, CB, TO
   c. Collection of Data: NP, LL, SY, CB, TO
   d. Management: SY, CB, TO
   e. Analysis: NP, LL, TO
   f. Interpretation of Data: NP, SY, CB, TO
   g. Preparation: NP, TO
   h. Review: NP, SY, CB, TO
   i. Approval of Manuscript: TO

d. Other Acknowledgments: none
Literature Cited


Figure Captions:

Figure 1: Color fundus photograph and fluorescein angiogram demonstrating a large choroidal neovascular complex with surrounding secondary radial chorioretinal folds in a case with age related macular degeneration.

Figure 2: Color fundus photograph of chronic bilateral chorioretinal folds with retinal pigment epithelial hyperplasia along with areas of atrophy that accompany the folds. Fluorescein angiogram shows corresponding areas of window defect and staining with no late leakage in a case of hyperopia.

Figure 3: Top: Chorioretinal folds in a patient with an orbital mass demonstrating the characteristic pattern of alternating hyper- and hypofluorescent bands. Note the pattern of the chorioretinal folds, suggesting irregular posterior contour. Bottom: Similarly alternating chorioretinal folds in a patient with chronic chorioretinal folds. There are focal areas of Bruchs staining along the crest of the folds that corresponding to early degeneration of the retinal pigment epithelium.

Figure 4: This case represents the most characteristic example of chorioretinal fold related maculopathy. In this case associated with chronic hyperopia (+ 5 diopters), the patient had long-standing chorioretinal folds and a yellowish, luteal appearance in the fovea. The fluorescein angiogram demonstrates early stippled hypofluorescence with late staining and some mild leakage. This appearance is very similar to the angiographic pattern seen in occult choroidal neovascularization referred to as late leakage of undetermined source.

Figure 5. The right eye of a patient with rheumatoid arthritis, possible posterior scleritis, and chronic chorioretinal folds with early hypofluorescence (top right), stippled hyperfluorescence in the mid-phase (bottom left) and late staining and leakage in the late phase (bottom right). This chorioretinal folds-related maculopathy resembles the fluorescein angiographic appearance described in occult choroidal neovascularization in age related macular degeneration.\textsuperscript{16}

Figure 6. In the left eye of this patient, the fluorescein angiogram also has stage 3 chorioretinal folds-related macular changes (top right) while the mid and late phase of the indocyanine green angiogram (bottom) does not demonstrate evidence of angiographic leakage.\textsuperscript{15}

Figure 7: Spectral domain ocular coherence tomography images before and after a single injection of intravitreal ranibizumab demonstrating complete resolution of an extrafoveal subretinal neovascular complex in a case with idiopathic chorioretinal folds.
Table 1: Baseline Demographics and Systemic Associations with Chorioretinal Folds

<table>
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<th>Total number of patients</th>
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<tr>
<td>Total number of eyes</td>
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<td>Mean follow-up ± SD (months)</td>
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<td>Range (months)</td>
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<td>Mean age ± SD (years)</td>
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SD= Standard Deviation; C= Caucasian; AA= African American; NR= Not Recorded; Y= Yes; N= No; Note that there is some overlap of cases (i.e. posterior scleritis and rheumatoid arthritis, hypertension, etc.)

aPresence of condition not recorded in all reviewed cases
Table 2. Comparisons between 3 angiographic patterns of chorioretinal folds

<table>
<thead>
<tr>
<th>Angiographic Description</th>
<th>Group 1 (n=8)</th>
<th>Group 2 (n=6)</th>
<th>Group 3 (n=8)</th>
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<tbody>
<tr>
<td>Description</td>
<td>Alternating bands of hyper and hypofluorescence without any staining or leakage</td>
<td>Areas of staining at the crest of the folds</td>
<td>Stippled hyperfluorescence expanding in the late frames</td>
</tr>
<tr>
<td>Age</td>
<td>56 ± 17 years</td>
<td>64 ± 21 years</td>
<td>68 ± 12 years</td>
</tr>
<tr>
<td>p-value</td>
<td>p &lt; 0.01</td>
<td>p = 0.2</td>
<td>(reference)</td>
</tr>
<tr>
<td>Gender</td>
<td>Male: 5, Female: 3</td>
<td>Male: 5, Female: 1</td>
<td>Male: 6, Female: 2</td>
</tr>
<tr>
<td>Initial Visual Acuity</td>
<td>20/80 (Range: 20/25-20/400)</td>
<td>20/50 (Range: 20/20-20/400)</td>
<td>20/60 (Range: 20/20-20/400)</td>
</tr>
<tr>
<td>Final Visual Acuity</td>
<td>20/80 (Range: 20/25-20/600)</td>
<td>20/50 (Range: 20/20-20/1000)</td>
<td>20/100 (Range: 20/20-20/500)</td>
</tr>
<tr>
<td>Treatments</td>
<td>None</td>
<td>None</td>
<td>Retroretinal Steroids (n=2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Intravitreal anti-VEGF agent (n=2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Photodynamic therapy (n=1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Submacular surgery (n=1)</td>
</tr>
<tr>
<td>Follow-up</td>
<td>11 ± 17 months (Range 0-41 months)</td>
<td>6 ± 12 months (Range 0-31 months)</td>
<td>23 ± 24 months (Range 3-79 months)</td>
</tr>
</tbody>
</table>
Timothy W. Olsen MD is serves as the F. Phinizy Calhoun Sr. Professor of Ophthalmology, Chairman of the Department of Ophthalmology at Emory. He completed both undergraduate and medical school at the University of Kansas, residency training at the University of Minnesota, and Fellowship in Vitreoretinal Diseases and Surgery at Emory. He began his academic career at the University of Wisconsin, founded the Minnesota Lions Macular Degeneration Center and then returned as chairman at Emory.