Choroidal Confusion: The Pachychoroid Spectrum of Diseases

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ABSTRACT

A 59-year-old African-American male presented for a comprehensive eye examination. His pertinent ocular history was extensive and included a past occurrence of Central Serous Chorioretinopathy (CSCR) in the left eye (OS), presumed macular toxicity of the right eye (OD) due to Plaquenil therapy for Rheumatoid Arthritis, and presumed Advanced-stage Dry Age-related Macular Degeneration (ARMD) of both eyes. Stargardt's Disease was also listed as a differential diagnosis under his ocular history. Upon clinical review and additional ancillary testing, we determined that the patient did not have Macular Degeneration, Stargardt's, or Plaquenil toxicity, and instead exhibited a pachychoroid disease. The pachychoroid spectrum is often overlooked by clinicians as it is a group of conditions and therefore can masquerade as several common diseases, such as ARMD, Bull's eye maculopathy, and Stargardt's Disease. The use of Optical Coherence Tomography (OCT) and Fundus Autofluorescent (FAF) photography helps in distinguishing among these differentials to rule-in a pachychoroid disease. Understanding these conditions can help avoid misdiagnoses and allow for more appropriate management of these patients.

KEY WORDS:
Choroid, Central Serous Chorioretinopathy (CSCR), fundus autofluorescence, Optical Coherence Tomography (OCT), Pachychoroid

INTRODUCTION

The term pachychoroid spectrum was coined by Warrow and colleagues in 2013. The conditions in this spectrum all display a thickened choroid and changes in the retinal pigmented epithelium (RPE), which may or may not be associated with retinal abnormalities.[1] This spectrum of diseases includes Pachychoroid Pigment Epitheliopathy (PPE), Central Serous Chorioretinopathy (CSCR), Pachychoroid Neovasculopathy (PNV), and Polypoidal Choroidal Vasculopathy (PCV).[1] These diseases can often be mistaken for several other conditions with similar presentations (Table 1) such as Stargardt's Disease, Age-Related Macular Degeneration (ARMD), and Bull's Eye Maculopathy, as demonstrated by the patient in this case report.

The choroid has several functions that contribute to the overall well-being of the eye including supplying the outer retina with essential nutrients and oxygen, aiding in thermoregulation, assisting in drainage of aqueous via the uveoscleral pathway, and absorbing light. The choroid consists of the innermost layer, Bruch's Membrane, the highly fenestrated choriocapillaris, two vascular layers (Haller's Layer and Sattler's Layer), and the suprachoroid.[2]

At birth, the choroid is about 200μm thick, and by age 90 it decreases in size to approximately 80μm.[2] Choroidal thickness is variable and is attributed to axial length, age, and ethnicity, with an average thickness in adults ranging from 191 to 354μm at the fovea.[1] The term "pachychoroid" is used when choroidal thickness exceeds 390μm.[1]

Choroidal thickness can be measured by using Enhanced Depth or Swept Source Optical Coherence Tomography (OCT) and retinal changes can be found and documented with Fundus Autofluorescence (FAF) imaging. The use of these imaging modalities can help distinguish between the various retinal and choroidal diseases to ensure correct diagnoses and allow for more accurate management of these patients.

Table 1 : *Differentials for this case report*

Differentials	Pathophysiology	Diagnosis	Typical Presentation
Pachychoroid Disease[2]	See Discussion	Clinical presentation, OCT, FAF, ICG	Choroidal thickening in the presence or absence of retinal abnormalities with associated RPE changes
Stargardt's Disease[7]	Mutation of ABCA4 Gene	Genetic Testing	Bilateral atrophic damage with clumps of lipofuscin
Bulls-Eye Maculopathy (Associated with Plaquenil use)[8,9]	Toxic retinopathy due to toxicity to retinal ganglion cells and binding of melanin in the RPE	Clinical examination supplemented by OCT and Visual Field	Bilateral mottled RPE and dull foveal reflex with hypofluorescent ring surrounded by hyperfluorescence
Geographic Atrophy/ Macular Degeneration [10]	Advanced-Stage Dry ARMD thought to be caused by oxidative stress leading to retinal cell death. Other factors: Poorly regenerating RPE and inflammation due to compromised complement cascade	Clinical examination supplemented by OCT and FAF More likely to progress to GA if large drusen, pigment changes, and/or soft indistinct drusen are present.	Usually bilateral, typically well demarcated atrophic areas in the macula with increased visibility of choroidal vasculature

CASE REPORT

A 59-year-old African-American male presented with a chief complaint of trouble with glare while driving at night and frequent tearing of both eyes. His ocular history included a past occurrence of CSCR in the left eye, macular RPE damage in the right eye greater than that in the left eye presumably due to macular toxicity secondary to prior treatment with Plaquenil for Rheumatoid Arthritis (from 09/2006 to 02/2011), and presumed AMD of both eyes. The patient's history was also remarkable for a differential diagnosis of Stargardt's, given his past clinical presentation. However, this diagnosis had not been confirmed by genetic testing.

The patient's best corrected visual acuity was Counting Fingers (CF) at 2 feet OD and 20/20 OS. No afferent pupillary defect (APD) was noted. His intraocular pressures (IOPs) were 18 mmHg OD and 15 mmHg OS. Slit lamp examination revealed trace cortical and nuclear lens changes OU and was otherwise unremarkable. Visual field testing showed a depressed field with a greatest density superior nasally, which was not consistent with macular toxicity (see Fig. 3).

Upon dilated fundus examination, a central area of macular atrophy with scattered drusen throughout the posterior pole OD, along with a pigment epithelial detachment, was noted along the superior temporal arcade. His left eye was remarkable for a vertical gravitational pooling pattern of atrophy temporal to the optic nerve head with scattered pinpoint drusen. An OCT scan through the macula showed a significantly thin fovea with loss of the outer retinal layers parafoveally extending a few disc diameters inferiorly OD. A normal foveal contour was noted OS with retinal thinning temporal to the optic nerve head (ONH), spanning from above the ONH and extending vertically down to five disc-diameters inferiorly. These findings are consistent with chronic damage from old CSCR and are in-line with the patient's prior ocular history. However, due to the patient's history of taking Plaquenil, these findings were attributed to retinal toxicity. This medication was discontinued in 2011 to decrease the risk of any further vision loss.

Based on our clinical findings and ancillary testing, we were able to rule out Macular Degeneration and Stargardt's Disease for this patient. The diagnosis of Bull's Eye Maculopathy secondary to Plaquenil use was also determined to not be the main cause of reduced vision as his retinal findings and visual field defects were documented only one month after initiating treatment and the findings were only in one eye. The FAF photos of his right eye displayed central macular atrophy with hyperfluorescent granulomas and a marked PED along the superior temporal arcade. The FAF photos of the left eye were remarkable for a gravitational vertical tracking pattern temporally, which is a classic presentation of a prior CSCR. Figure 1 shows FAF photos of the right and left eyes. Figure 2 exhibits Enhanced Depth Imaging (EDI) OCT of the patient's right eye, which revealed an above-average choroidal thickness of 464mm, supporting a diagnosis within the pachychoroid spectrum. These findings helped us re-assess the patient's clinical history and diagnose based on features consistent with a pachychoroid spectrum disorder. Since pachychoroid disease was not well documented prior to 2013, it was not considered to be a differential at the time of diagnosis for this patient in 2011.

Figure 1a: *Fundus photos of the right eye, captured in 2018 with fundus autofluorescence and color photography. FAF photo exhibits central macular atrophy with hyperfluorescent granulomas.*

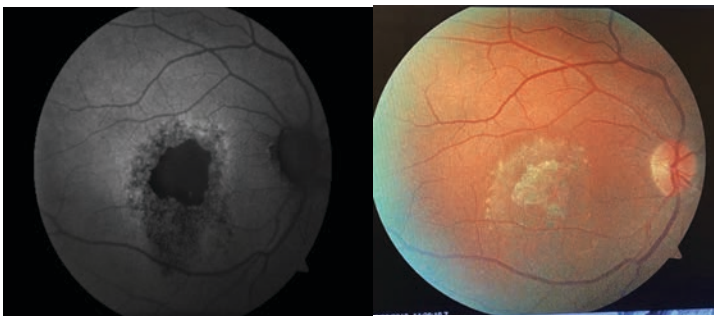


Figure 1b: *Fundus photos of the left eye, captured in 2018 with fundus autofluorescence and color photography. Note the gravitational vertical pooling temporal to ONH, a classic presentation of a prior CSCR.*

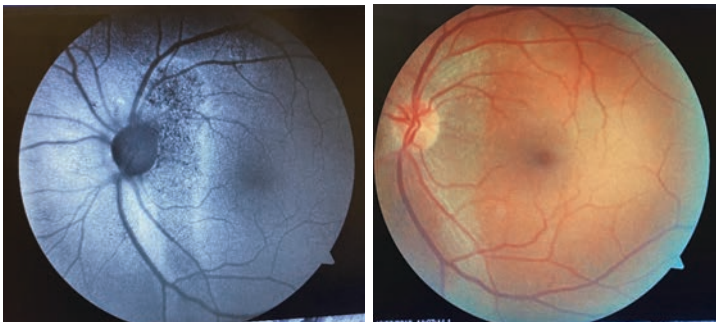
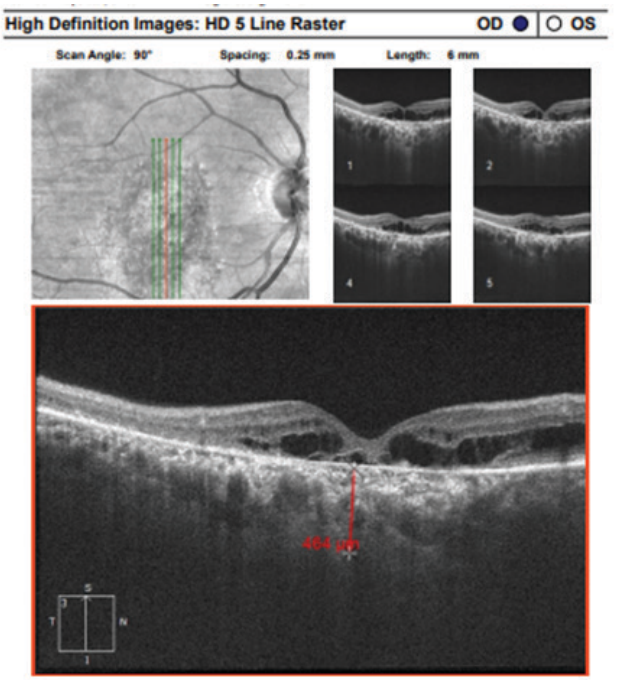


Figure 2: *An EDI OCT of the patient's right eye exhibits an above-average choroidal thickness of 464um, supporting a diagnosis within the pachychoroid spectrum.*



We scheduled the patient for a 6-month follow-up to repeat his OCT, which revealed cystic fluid pockets within the macula and worsening of the left vertical tracking temporal to the optic nerve head in the left eye. His vision was stable in both eyes. He was referred to our retinal specialists for evaluation and treatment of intraretinal cystoid fluid. Management for the patient at this stage of his condition was focused on having him start Dorzolamide BID in hopes of decreasing the cystic fluid. We are now also focused on ensuring best corrected vision and protection of the patient's good eye with polycarbonate spectacle correction. Due to the patient's visual condition, he is being monitored closely by a retinal specialist at this time. The patient will be monitored with FAF photos and macular OCTs as indicated. Ophthalmology also suggested an evaluation at the Scheie Eye Institute. While an atypical presentation of CSCR is likely, the patient was advised to consider genetic testing and to undergo ERG to rule out any hereditary dystrophy.

DISCUSSION

The pachychoroid spectrum of diseases consists of several types of conditions that arise from an abnormal choroid. These include Pachychoroid Pigment Epitheliopathy (PPE), Central Serous Chorioretinopathy (CSCR), Pachychoroid Neovasculopathy (PNV), and Polypoidal Choroidal Vasculopathy (PCV).[1]

Pachychoroid Pigment Epitheliopathy is typically a silent disease that may be a precursor to CSCR. Upon clinical examination, a reddish orange fundus may be observed with reduced tessellation and small serous pigment epithelial detachments (PEDs). These can be visualized with an OCT. Variable pigment alteration may also be noted.[3]

CSCR can be acute or chronic and is one of the more common Pachychoroid diseases. CSCR involves a serous detachment of the neurosensory retina. This condition typically presents in otherwise healthy young adults. Type A personality, stress, pregnancy, and corticosteroid usage have been linked to CSCR.[1] A patient will often have an acute presentation with a positive scotoma, metamorphopsia, and sudden, painless blurred vision.[4] Clinical examination will reveal a raised area in the macula with hypo- or hyperfluorescent changes that can be seen on FAF. A typical case of CSCR resolves in about 3 to 6 months without treatment. However, a case lasting longer than 12 months should be considered chronic and referred for treatment. Chronic CSCR causes more severe harm as the retina is swollen for a prolonged period, which leads to RPE damage and puts the patient at an increased risk of developing Choroidal Neovascularization (CNV) and macular atrophy.[3] There is no gold standard treatment for chronic CSCR. Treatments such as Photodynamic Therapy (PDT), Beta Blockers, Carbonic Anhydrase Inhibitors, and Focal Laser have all been studied as treatment options with variable degrees of success.[5]

Pachychoroid Neovasculopathy may develop as a sequela of PPE and/or CSCR. The patient may have metamorphopsia with associated blurred vision. On OCT, a tangled network of vessels is observed with a classic "double layer sign," indicating a Type 1 CNV. This is due to prolonged PEDs and chronic RPE changes.[3]

Polypoidal Choroidal Vasculopathy is a longstanding variant of Type 1 CNV. FAF will reveal circular abnormalities with hypo-autofluorescent centers which are polyps, and hyper-autofluorescent surroundings. OCT can show variable PEDs which may be sharp and irregular. Clinical examination will reveal characteristic vessel hyalinization.

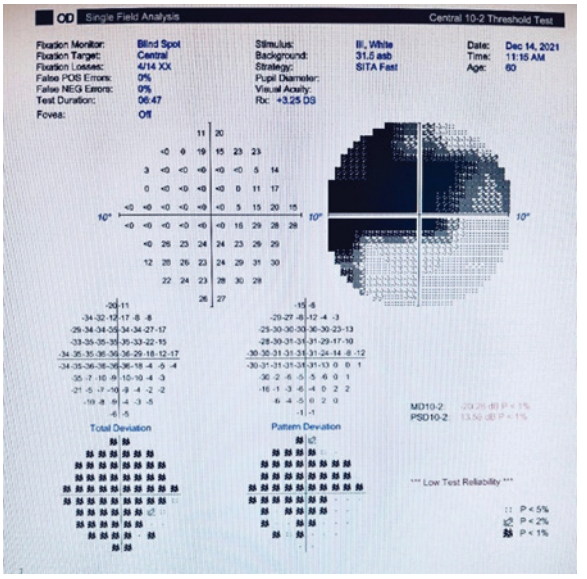
Fundus autofluorescence is a type of specialized testing that can aid in diagnosing a pachychoroid disease. FAF photography operates in the blue-green spectrum of visible light to provide a density map of lipofuscin, which is the dominant macular fluorophore. It absorbs blue light at 470 nm and emits yellow–green light at 600–610 nm. The fluorescent characteristics of lipofuscin produce images that provide a clinical picture that is different from more conventional imaging techniques. As the presence of lipofuscin indicates RPE damage, this form of documentation is critical in patients with conditions that tend to target the RPE.[6]

There are two types of OCT technologies that provide comprehensive imaging of the choroid: Enhanced Depth Imaging (EDI) OCT and Swept-Source OCT. EDI OCT produces an inverted mirror image of the retina. EDI OCT allows the choroid to fall closer to the zero-delay line, increasing signal strength and providing a higher definition scan of the choroid which allows providers to physically measure the choroidal thickness by observing the choroid-scleral junction interface. Swept-source (SS) technology is newer; it uses a 1050 nm wavelength and a scanning speed of 100,000 A-scans/second. The faster scanning speed lessens distortion due to eye movements. Patient comfort is increased due to the longer wavelength being invisible. As a reference, standard OCT uses wavelengths in the 800 nm to 870 nm range, with less signal strength to image the choroid.[7]

Upon record review for our patient, abnormal RPE findings (along with a small central defect on HVF 10-2, OD only) were noted only one month after the patient was started on Plaquenil 200mg BID. Based on a review of the

literature, this is not enough time for this drug to lead to the development of macular toxicity; a much higher accumulation is needed for toxicity and a subsequent central defect. Additionally, it is unusual to find a unilateral presentation of Plaquenil toxicity; most cases present bilaterally. Figure 3 shows visual-field findings of the right eye. The 2016 AAO guidelines state that the overall prevalence of toxicity in a 5-year study population is 7.5% after 5 years of Plaquenil treatment. This risk depends on the daily dosage and duration of use. If the patient is taking the recommended dosage (5.0mg/kg/day of real body weight), the risk of toxicity is <1% for up to five years and <2% for up to 10 years.[4] In 2006, our patient weighed 185 pounds (83.9 kg), which made 200 mg BID an appropriate dosage for him and placed him at a low risk for developing toxicity.

Figure 3: *Visual Field OD. The patient's right eye visual field exhibits a depressed field, densest superior nasally, which is not consistent with macular toxicity.*



Since OCTs were not readily available in the early 2000s, it was difficult to fully assess the RPE and choroid. The term "pachychoroid diseases" was not coined until 2013, which explains why this was not used as a differential diagnosis at the time. Additionally, the patient was put on a 10-day course of Prednisone 10mg QD in March 2007, which was just a few months before when retinal findings were first noted. As steroid use is a risk factor for PPE and CSCR, this further confirms the diagnosis to be in the pachychoroid spectrum of diseases.

Due to the period of time the patient was treated with Plaquenil prior to macular damage being noted, unilateral presentation, use of oral steroids for a few months prior to retinal damage, and subsequent presence of CSCR in the other eye and thickened choroid, the findings were most consistent with a pachychoroid spectrum disorder. We hypothesized that the patient suffered from a prior occurrence of chronic CSCR in his right eye that left the macula damaged with vision loss as the only management performed at that time was discontinuing Plaquenil. We also considered other factors that helped us exclude his previous diagnosis of ARMD such as his age and African-American descent.

This patient had several previously diagnosed ocular conditions, which made it difficult to identify what exactly caused the devastating vision loss in his right eye. The use of specific testing modalities allowed us to support our clinical findings and provide us with more data to help provide a more definitive diagnoses. It is our role as primary eye care providers to be able to gather this data to help distinguish between diseases to ensure our patients are receiving the best care and most appropriate management for their specified diagnosis. ●

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