Ocular Manifestations of Lupus Erythematosus

Mark L. Landig, OD; Pauline F. Ilsen, OD, FAAO

Abstract

Background: Lupus erythematosus (LE) is a chronic autoimmune disease that elicits a type III hypersensitivity reaction in which antibody-immune complexes precipitate and causes further immune response. There are three types of LE: discoid, systemic, and drug-induced. Systemic lupus erythematosus (SLE) is among the most common and concerning of the three. SLE harms mostly the heart, joints, skin, blood vessels, liver, kidneys, and nervous system. In addition to systemic issues, LE uniquely manifests itself in and around the eye. Secondary Sjögren's syndrome (SS) and severe dry eyes are common among LE patients. Currently, there is no cure for LE; patients are often treated with an immunosuppressant or antimalarials, such as hydroxychloroquine. Case Reports: A patient who appeared to have discoid lupus erythematosus (DLE) with secondary SS was referred to eye clinic by rheumatology for hydroxychloroquine screening. He presented with severe dry eyes. Treatment for dry eyes was initiated and screening for hydroxychloroquine toxicity was conducted. Another patient presented to the eye clinic for reduced vision in his right eye. He was diagnosed with systemic lupus with no treatment. Ophthalmic examination revealed a unilateral macular edema secondary to a central retinal vein occlusion likely to active systemic lupus. Immediate referral to rheumatology and ophthalmology was made. Conclusion: Since patients with LE may have many ocular manifestations, optometrists should be able to recognize them and ensure that the patient receives appropriate treatment. Communication with ophthalmology and rheumatology is important for the management of these cases.

Introduction

Lupus erythematosus is a chronic inflammatory disease that affects the body in multiple levels, targeting different organs. There are three different types of lupus erythematosus: skin, known as discoid lupus; drug-induced; and systemic lupus.1 Discoid lupus is often diagnosed after biopsy of a rash that manifests on the face, neck, or scalp.1 Cases of discoid tend to be limited to the skin, but may also have symptoms which manifest systemically. Certain prescribed medications can induce similar symptoms to those of systemic lupus, known as drug-induced lupus. Medications that are known to cause drug-induced lupus are: hydralazine — a direct acting smooth muscle relaxant, procainamide — an antiarrhythmic agent, and isoniazid — an anti-tuberculosis medication.1 The mechanism is unclear, but some theories include abnormal oxidative drug metabolism, the drugs may act as haptons, and/or drugs may nonspecifically activate lymphocytes.2

Systemic lupus erythematosus is the most common form and tends to be the most severe type of lupus; it can affect any organ in the body.1 The skin, joints, blood, kidneys, lungs, and the heart are some examples of organs that are vulnerable.1,2 This review will mainly focus on systemic lupus, but it is important for optometrists to understand that there are other types of the disease.

The prevalence of SLE is 40 cases per 100,000 persons among Northern Europeans to more than 200 per 100,000 persons among African-Americans.1 In the United States, the number of people diagnosed with lupus has reached to at least 250,000.2 The cause of lupus is still unknown, but studies have shown that a genetic predisposition and the environment play important roles in the disease process.1,2 Environmental factors that are known to stimulate the disease process include, but not limited to, ultraviolet radiation, infection, antibiotics in particular sulfa and penicillin family, stress, hormones, and drugs.1,2

Case 1

A 66-year-old African-American male was referred to the eye clinic by rheumatology for his annual hydroxychloroquine eye screening. He reported no changes in his vision in the past year. He was diagnosed with discoid lupus and Sjögren syndrome 14 years ago. His body mass index (BMI) was about 29 and his weight was 191 pounds. His dry mouth and dry eyes were controlled with oral pilocarpine and carboxymethylcellulose eye drops, respectively. In his last rheumatologic examination, he denied any oral ulcers, sun sensitivity, Raynaud’s arthralgia, alopecia, abdominal pain, or new skin rash involvement elsewhere. He maintained a regular exercise regimen and was eating well.
His medical history was remarkable for discoid lupus erythematosus, tinea unguium, nocturia, Sjögren syndrome, and hearing loss. His most recent blood pressure was 112/81 mmHg. Medications included carboxymethylcellulose 0.5% solution instilled 4 times daily for dry eyes, cholecalciferol 1000 unit tablet for bone strengthening, gabapentin 300 mg for nerve pain, hydroxychloroquine sulfate 200 mg for lupus, and pilocarpine HCl 5 mg for dry mouth. He applied sunscreen-35 PABA-free combination cream on the affected areas every 2 to 3 hours when out in the sun.

He had a positive biopsy of the skin, negative antinuclear antibody (ANA), and positive Sjögren’s syndrome A (SSA). He was followed by his rheumatologist every 6 months. Tables I and II show his pertinent laboratory test results.

Ophthalmic examination revealed best-corrected visual acuities of 6/6 (20/20) OD and 6/6 (20/20) OS. Pupils were round, equal and reactive to light. Extraocular muscles were smooth, accurate, full and extensive. Cover tests was orthophoria at distance and 4 exophoria at near. His confrontation fields were full to finger counting.

On exterior exam, he had a small, approximately 5 mm in size rash, on his right hand and an 8 mm elliptical shape rash above his left lip (Fig. 1). Findings in the anterior segment examination were all within normal limits for his age with the exception of grade 1 superficial punctate keratopathy and reduced tear breakup time to 4 seconds for both eyes. He has non-Visually significant cataracts OU. Schirmer’s test with anesthesia was performed at this visit and was mildly reduced to 13 mm right eye and 14 mm left eye. His intraocular pressure was 15 mmHg both right and left eye at 11:30 a.m. with Goldmann applanation method.

Posterior segment examination was within normal limits. View in was clear. Optic nerve head was average in size, pink and healthy with distinct margins. The cup-to-disc ratio was measured to be 0.50 round on both right and left eye. His retinal blood vessels were of good caliber.

His Humphreys central 10-2 visual field revealed no paracentral scotoma. Spectralis optical coherence tomography (OCT) showed appropriate foveal contour, intraretinal layers were intact, and the RPE/Bruch’s complex was intact (Figs. 2, 3). All 14 color plates (Ishihara) were correctly identified when tested monocularly. Since his dry eyes and dry mouth were controlled well with pilocarpine pills and carboxymethylcellulose eye drops, he was instructed to continue using them and to return for routine follow-up in 1 year.

**Case 2**

A 24-year-old Asian-American male patient reported for his yearly eye examination requesting new eyeglasses. He reported moderate visual changes in his right eye that started 7 days ago.
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His ocular history was significant for moderate dry eyes and myopia. His medical history was remarkable for systemic lupus erythematosus, hypertension, neck pain, hyperlipidemia, and acute renal impairment. He had arthritis, malar rash, Raynaud’s phenomenon, and proteinuria. He had several systemic signs of lupus flare: low-grade fever, polyarthritis, and diarrhea. Systemic medications included aspirin, atovaquone to prevent infection; cholecalciferol for vitamin D supplementation; docusate sodium for constipation; furosemide for water retention; gabapentin and hydrocodone for pain; Lisinopril for blood pressure; simvastatin for cholesterol; and sunscreen-35 PABA-free combination for sun protection. He had no significant family ocular history. He denied any headache, eye trauma, or ocular surgery in the past. Table III shows a summary of significant laboratory test results.

Ophthalmic examination revealed reduced best-corrected visual acuities of 6/30 (20/100) OD and 6/6 (20/20) OS. A pinhole did not improve the visual acuity of the right eye. Pupils were round, equal, and reactive to light with no relative afferent pupillary defect. His extraocular muscles were smooth, accurate, full and extensive. Ocular alignment was orthophoria at distance and near. Confrontation fields were normal to finger counting. Gross assessment of his orbits revealed no evidence of trauma, ptosis, and Hirschberg were centered in both eyes. Slit lamp biomicroscopy showed grade 1 meibomian gland dysfunction and mild blepharitis, with unremarkable findings for the conjunctiva, sclera, iris, anterior chamber, and lens OU. The right cornea revealed diffuse punctate epithelial erosions and reduced tear breakup time to 8 seconds both eyes. Color vision test and visual fields were not tested at the initial visit.

Dilated fundus examination revealed normal, well perfused discs, with a cup-to-disc ratio of 0.30 round on both eyes. The macula of the right eye appeared to be elevated with no foveal reflex, while the left eye was flat and intact. Spectralis macular OCT scan revealed an increased central macula thickness of 319 microns of the right eye and normal 283 microns of the left eye. There were many scattered cotton wool spots and dot-blot hemorrhages throughout the posterior pole of the right eye, while the left eye was homogenous. The peripheral retina was attached 360 degrees with no holes, tears, or breaks (Figs. 4, 5).

A diagnosis of macular edema secondary to a central retinal vein occlusion likely due to an inflammatory process such as lupus was made. The patient was referred to rheumatology immediately for an evaluation of his lupus and he was scheduled for a next-day follow-up with retina clinic. He was started on hydroxychloroquine 200 mg b.i.d. by mouth by rheumatology. After 8 months of close follow-up with rheumatology, his macular edema resolved. He was corrected to 6/6 (20/20) in both right and left eyes with a low myopic prescription (Fig. 6).

Discussion
Diagnosis of Lupus Erythematosus
The diagnosis of LE is contingent upon iconic clinical features and supportive laboratory results. Early in the disease process, patients who are suspected to have SLE often experience classic symptoms such as unexplained nonspecific fever, fatigue, or weight loss. A photosensitivity rash may develop on the skin, primarily in areas that are exposed to sunlight. Raynaud phenomenon, arthritis, lung and heart inflammation, and alopecia are examples of early manifestations. Primary care providers who have patients with these manifestations will typically order a panel of laboratory testing, including screening for specific auto-antibodies. Complete blood count (CBC), metabolic profile, creatine kinase, erythrocyte sedimentation...
rate, and urinalysis are the common laboratory tests that are often ordered. Autoantibody testing include, but not limited to, antinuclear antibodies, antiphospholipid antibodies, antibodies to double-stranded deoxyribonucleic acid (dsDNA), and anti-Smith (Sm) antibody. For further evaluation, biopsies of the affected organs may also be performed. For example, if discoid lupus is suspected, a skin biopsy may be done. Clinical features, laboratory results, and antibody testing are all key in determining whether or not a patient is positive for SLE; however, an approach that is often utilized by many rheumatologists to differentiate SLE from other systemic disease is a questionnaire (Table IV). If three or more questions are answered with a “yes,” SLE is a possibility and an ANA is warranted. Sometimes a patient may have had SLE for years but has remained undiagnosed for a variety of reasons. Primary care physicians and rheumatologists usually look for classic clinical signs: such as discoid rash, oral ulcers, and malar rash.

**General Pathophysiology**

Lupus is characterized as a type-III hypersensitivity reaction, which occurs when antigen-antibody complexes are not adequately cleared out by the innate immune system. There are many proposed mechanisms for lupus pathophysiology, making it a very complex disease. Lupus disease activity is thought to involve three main processes: activation of adaptive immunity, activation of innate immunity, and ineffective clearance of immune complexes.

When a cell undergoes apoptosis, it induces surface blebs, which leak intracellular content into the extracellular space. Due to the ineffective clearance in lupus patients, more DNA is released. T-cells recognize and bind with the major histocompatibility complex (MHC) molecule on the surface nuclear antigen-presenting cell. However, this binding is not strong enough to stimulate the T-cell. In this mechanism, there have been theories of co-stimulatory molecular pairs, such as CD40-CD40 ligand and CD28-B7, which generates the second signal in activating the T-cell. This, in turn, will activate the B cell, releasing antibodies, which is targeted for double-stranded DNA. Normally C4 of the complement system inhibits the production of self-antigen.

In lupus, complement system C1q, C2, C3 and C4 are deficient. Current researchers are looking into ways to inhibit the co-stimulatory molecular pairs as way to treat lupus. The normal action of the complement system is to promote immune response. The complement cascade ultimately forms C3b complex, an opsonin that promotes phagocytosis, and C3a, acting as a chemo-attractant for immune cells. If this complex fails, they eventually lead to the formation of membrane attack complex that lyses cells.

In addition to autoantibodies to dsDNA, SLE is also associated with autoantibodies to red blood cells (RBC), white blood cells...
(WBC), and platelets, which can lead to hemolytic anemia, leukocytopenia, and thrombocytopenia respectively.\textsuperscript{3,12,13}

If someone is diagnosed with lupus, physicians often recommend patients to stop smoking, as there is a strong correlation between smoking and the disease process. The most common treatment of lupus is hydroxychloroquine, an anti-malarial drug.\textsuperscript{5} Other treatment modalities are nonsteroidal anti-inflammatory drug, systemic corticosteroids, methotrexate, cyclophosphamide, and azathioprine.\textsuperscript{4-6}

**Ocular Manifestation of Lupus**

Systemic lupus erythematosus can affect the eye quite extensively, including the adnexa, corneal surface, retina, and optic nerve. More common findings among SLE patients are keratoconjunctivitis sicca (KCS) and, if the disease process is not controlled, retinopathy.\textsuperscript{14,15} According to Sobrin et al, there have been cases where an ocular manifestation has manifested well in advance of the definitive diagnosis of systemic lupus.\textsuperscript{16} However, ocular manifestation is not part of the diagnostic scoring scale.

**External Involvement**

The classic sign of discoid lupus is a raised, scaly lesion on the skin. The lesions may appear like chronic blepharitis if they appear around the eyelid.\textsuperscript{16} A definitive diagnosis of discoid lupus can be established after a biopsy has been performed and several conservative topical therapies have been applied with no resolution.\textsuperscript{15,16}

Keratoconjunctivitis sicca (KCS) is one of the most common ocular manifestation lupus patients may experience. According to Jensen et al, 12 out of their 20 patients with lupus reported at least one symptom of dry eyes.\textsuperscript{17} In a retrospective study of a cohort of 55 patients, KCS occurred in approximately 25% of patients.\textsuperscript{18} Other external manifestations that optometrists need to be mindful of are interstitial keratitis and conjunctivitis, though both are rare.\textsuperscript{17,18}

Episcleritis and scleritis are manifestation of SLE, and according to Sobrin et al, they can precede diagnosis of SLE by as much as 3 years.\textsuperscript{16} Necrotizing and nonnecrotizing scleritis may manifest, but necrotizing type is less common with SLE as compared to rheumatoid arthritis. According to Situla, the incidence of episcleritis in adults with SLE is 2.4%.\textsuperscript{19} In general, episcleritis is benign, with associated symptoms of red eye, dull sensation around the orbit, and tearing. Scleritis is more significant and is more of a concern for vision loss.\textsuperscript{16,19}

**Retinal Involvement**

Retinopathy is a common ocular manifestation among SLE patients. According to a prospective study by Stafford-Brady, 88% of patients with lupus retinopathy had active disease.\textsuperscript{20} Common clinical retinal findings are cotton wool spots (CWS), which are microinfarctions of the nerve fiber layer with the cessation of axoplasmic flow, resulting in accumulation of mitochondria.\textsuperscript{21} CWS may be isolated or associated hemorrhages may appear. Contrasting with hypertensive and diabetic retinopathies, where arteries tend to be tortuous, SLE retinopathy displays relative dilation of the arteries.\textsuperscript{22} Other findings consist of hemorrhages and vasculitis.\textsuperscript{22}

In Ushiyama et al’s clinical cross-sectional study of 69 patients, 7 of the 69 patients (10%) presented with retinopathy. In this study, the average age of onset of SLE with and without retinopathy was 34.2 and 31.9 years old, respectively.\textsuperscript{23}

Findings from this study shown that patients with retinopathy also presented with proteinuria and central nervous system (CNS) disease. From the seven patients with retinopathy, four of them presented with proteinuria (57%). According to the study, patients with retinopathy had higher chance of developing CNS disease: 71%, with retinopathy compared to 13%, without retinopathy. The study suggests that retinopathy tends to develop with SLE patients who have renal or CNS disease, or both.\textsuperscript{22,23}

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**Table IV. Questions for diagnosing systemic lupus erythematosus**

<table>
<thead>
<tr>
<th>Questionnaire</th>
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<tbody>
<tr>
<td>1. Do you have rheumatism or arthritis for at least 3 months?</td>
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<tr>
<td>2. Are your fingers uncomfortable in the cold or feel numb?</td>
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<tr>
<td>3. Have you had sores in the month for at least 2 weeks?</td>
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<td>4. Are you diagnosed with anemia, leukocytopenia, or thrombocytopenia?</td>
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<td>5. Have you had a rash on the face for at least 1 month and has not improved?</td>
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<tr>
<td>6. Do you have skin reaction after being in the sun?</td>
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<td>7. Do you have difficulty with taking deep breaths?</td>
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<tr>
<td>8. Do you have proteinuria?</td>
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<tr>
<td>9. Have you lost hair due to an autoimmune disease?</td>
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<tr>
<td>10. Have you had any seizure attack?</td>
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![Spectralis Macular OCT of the right and left after 8 months of close follow-up with rheumatology and hydroxychloroquine treatment. Best corrected visual acuity was 6/6 (20/20) in both right and left eye.](image-url)
The earliest manifestation of lupus retinopathy is hemorrhages and cotton wool spots. The pathogenesis is the deposit of immune complexes, such as immunoglobulin and complement deposits, in the vessel walls. Retinal vasculitis, inflammation of retinal arterioles and venules, tends to manifest in an acute process of the disease and in most cases has a poorer prognosis in terms of visual outcome. Hall et al’s study in 1984 reported the first positive antiphospholipid antibodies and retinal vasculopathy. Since then, more studies have supported a relationship between antiphospholipid antibody titer and the disease process. There has been a case report that identified central retinal artery/vein occlusion, vitreous hemorrhage, and neovascularization as a result of retinal vasculopathy in a lupus patient. Lupus retinopathy that leads to a central vein occlusion tends to manifest unilaterally. In Montecheromo et al’s study, among the SLE patients who had retinal involvement, 77% of them had positive antiphospholipid antibody titers, compared to patients who had no retinal involvement, of whom only 29% had positive titers.

Rarely does lupus retinopathy become proliferative, but when it does with severe vasculitis, visual prognosis is quite poor. According to Jabs et al, more than 50% of the affected eyes have visual acuity of 6/60 (20/200) or worse. With diffuse arteriolar occlusion and extensive capillary nonperfusion, retinal neovascularization will manifest. Often times the severity of retinopathy is linked directly to the activity of the disease process; however, there have been a few cases of proliferative retinopathy in patients with quiescent disease.

Immunosuppression has been shown to improve retinopathy. Unfortunately, visual acuity loss from severe retinopathy is permanent, due to retinal ischemia. In addition to immunosuppressant, other treatment that was utilized to help visual outcome presented in literature were plasmapheresis and plasma exchange. Vitrectomy, panretinal photocoagulation, intravitreal antivascular endothelial growth factor agents were used to treat retinopathy involving retinal ischemia. Retinal vein occlusion is rare in patients with SLE, but has occurred in several reported cases with active lupus retinopathy. In patients who have proliferative retinopathy, pan-retinal photocoagulation is warranted using the same criteria from diabetes and branch retinal vein occlusion. A new case study conducted by Doruk et al showed positive outcome both visually and anatomically with intravitreal ranibizumab injection prior to PRP.

**Choroidal Involvement**

According to Palejwala, lupus choroidopathy is a rare finding, with only about 40 patients reported in the literature. Lupus choroidopathy is often linked to significant nephropathy, uncontrolled blood pressure, and CNS vasculitis. Sophisticated ocular imaging, such as Indocyanine green angiography (ICG) has been utilized to identify a change in choroidal circulation in patients who have active lupus. Fluorescein angiography demonstrates areas of focal early transient hypofluorescence, intermediate and late diffuse choroidal hyperfluorescence along with distortion of the large choroidal vessels. One study discussed six patients with active lupus who had multifocal serous elevation of the retina pigment epithelium (RPE) and sensory retina. Improvement of the serous detachment in three patients occurred with control of the systemic disease. Another study showed two cases of active lupus and correlation of multifocal RPE and serous retinal detachments. One of these patients showed deposits of immune complexes in Bruch’s membrane leading researchers to believe that the insult was due to anti-RPE antibodies.

Using ICG, Baglio et al discovered a relationship between choroidopathy and active nephropathy. This finding was significant; however, several studies indicated that the pathophysiology of choroidopathy is multifactorial: uncontrolled hypertension, antiretinal pigment epithelium antibodies, and immune complex deposition into the choriocapillaris. Choroidopathy has been shown to respond to corticosteroids and immunosuppression. Choroidopathy is a good indication of aggressive disease process and systemic work-up is warranted with a rheumatologist.

**Neuro-Ophthalmic Involvement**

Optic nerve disease is possible in severe disease and manifests as optic neuritis or ischemic optic neuropathy, and occurs in about 1% of patients. Patients who have optic neuritis due to lupus will have very poor visual acuity, most of them will see worse than 6/60 (20/200). Optic neuritis secondary to lupus is different compared to that of optic neuritis secondary to multiple sclerosis (MS). Lupus induced optic neuritis is thought to be an ischemic process that leads to demyelination and axonal necrosis, which directly correlate to vision. In MS patients, the primary cause of optic neuritis is the inflammation causing a demyelinating process. The Optic Neuritis Treatment Trial (ONTT), 87% of patients recovered better than 6/7.5 (20/25) at 5 years follow-up. Comparing it to Lin et al study, only 50% of patients recovered to visual acuity better than 6/7.5 (20/25); 37.5% remained worse than 6/60 (20/200). Similar to optic neuritis due to MS, optic neuritis secondary to lupus responds well with high dose corticosteroids. Optic neuropathy is possible if the small blood vessels supplying the optic nerve head and retrolubar nerve are affected by the lupus disease process. Patients may complain of a sudden vision loss and visual field testing will show altitudinal field loss. Optic neuropathy may or may not be associated with disc edema. Optic neuropathy often occurs bilaterally and responds well with high dose intravitreal corticosteroids following taper.

Ocular motility can also be affected in the active disease process. According to Keane et al, eye movement abnormality has been reported in about 29% of patients. The cause is microvascular disease in the brainstem. Intern clear ophthalmoplegia is the most common cause of conjugate gaze abnormalities, while sixth nerve palsy is most common among dysconjugate gaze abnormalities.
**Ophthalmic Side Effects from Treatment**

Treatment for lupus can also cause ophthalmic morbidity, and optometrists need to be aware of what to watch for when patients are undergoing certain therapies. Corticosteroids are often used to treat lupus and may cause cataracts and steroid-induced glaucoma. Another treatment modality that is very popular in the rheumatology community is hydroxychloroquine. If a patient is susceptible to hydroxychloroquine toxicity, and no intervention is done, irreversible blindness can result.\(^{28,29}\)

**Hydroxychloroquine Toxicity**

The American Academy of Ophthalmology recommendation for screening of chloroquine (CQ) and hydroxychloroquine (HCQ) retinopathy were updated in 2011 with improved screening tools and new knowledge on the prevalence of the retinopathy. The prevalence of toxicity within the first 5 years of use was quite low and increased after 5 to 7 years of HCQ use or a cumulative dose of 1000 g to 1%.\(^{49}\) The risk is even higher after 15 to 20 years of use. One study found that risk increases 4 times after 7 years of use.\(^{50}\) In a retrospective medical record review performed at Doheny Eye Institute at the University of Southern California and at Northwestern University Sorrel Rosin Eye Center in Chicago, the average mean age toxicity development was 10.4 years, with a range of 3 to 10 years.\(^{51}\) There are also other factors that optometrists should be aware of that may increase the risk of retinopathy. Some risk factors include the duration of more than 5 years of use; cumulative dose of greater than 1000 g of HCQ and greater than 460 g of CQ; daily dose exceeding 400 mg/day of HCQ and greater than 250 mg/day of CQ; complications with the kidney or liver; and current presentation of maculopathy.\(^{49,51,52}\)

The classic sign of toxicity is bilateral bull’s eye maculopathy. During funduscopic examination, there will be a ring of RPE depigmentation that spares a foveal island. The mechanism of CQ and HCQ toxicity is not fully understood but scientists have speculated that both drugs have a sudden effect on metabolism of retinal cells as they both bind to melanin in the retinal pigment epithelium (RPE) and this binding is known to limit the retina and stabilize the photoreceptor layer with improvement in visual function.\(^{51}\)

The American Academy of Ophthalmology (AAO) recommends performing a baseline examination within 1 year of initiating treatment and annual screenings after 5 years of treatment in all patients. Humphrey central 10-2 visual field is recommended because it is readily available and can elucidate the degree of functional loss.\(^{51}\) Marmor et al emphasized the importance of a 10-2 visual field; their study concluded that about 10% of patients who had early HCQ toxicity showed a ring scotoma on the visual field in spite of a normal macular spectral domain OCT.\(^{51}\) Among the 2,000 patients who were enrolled in the study from Stanford and Kaiser Permanente who had used HCQ with cumulative doses larger than 1000 g, 150 had toxicity.\(^{53}\) All 2,000 patients had no history of macular disease.\(^{53}\)

In addition to a 10-2 visual field, objective testing is also recommended. Spectral domain OCT (SD-OCT) is recommended since it is widely available, sensitive, and easy to use. Multifocal electroretinogram (mfERG) and fundus autofluorescence (FAF) are also sensitive and can detect early changes; however, their availability is sparse.\(^{52,54}\) Furthermore, the relative sensitivity and specificity have not been fully established with these tests.\(^{53}\)

If a patient presents with new visual symptoms or any abnormalities are revealed with screening tests, a more careful evaluation is warranted. If a patient presents with possible early toxicity, the patient may elect to discontinue the medication with consultation with a rheumatologist, or to be monitored in 3- to 6-month intervals until there is enough evidence to rule out toxicity. Currently there is no definition of “early toxicity,” so any changes in the macula, especially the parafoveal regions, and changes in visual field should be taken seriously.\(^{51}\) If a patient presents with probable toxicity or “clear evident toxicity,” a consultation with the patient’s rheumatologist needs to be done immediately with recommendations to discontinue the medication.\(^{52,53}\) Manifestation of toxicity or clearly evident toxicity is defined as having either bilateral bull’s eye scotoma, bilateral paracentral mfERG, bilateral depigmentation, or parafoveal abnormalities on fundus autofluorescence.\(^{52}\) There should be a close follow-up regimen of 3 months to assess the progression and ensure that the patient understands the risks of the medication.\(^{52,56}\) Patients with probable toxicity would benefit with fullfield ERG and referring patients to medical centers who can perform such tests is recommended. When medication is discontinued, the patient should be re-examined in 3 months after discontinuation and then annually until findings are stable.\(^{52}\)

**Conclusion**

Ocular manifestations of lupus may be sight-threatening and can be an indicator of active disease. Very close follow-ups are warranted for patient who has active disease or history thereof. Ocular pain or a decrease in visual acuity warrants an immediate consultation with an eye specialist. The serious manifestations such as scleritis, lupus retinopathy, and choroidopathy need systemic work up. As primary eye care providers, one needs to identify when an appropriate, timely referral to a rheumatologist for SLE workup is warranted.\(^{56}\)

When HCQ therapy is utilized, patients should be educated extensively regarding the importance of regular check-ups. Patients need to be advised to return to clinic with new visual symptoms, including, but not limited to the following: a decrease in visual sensitivity, reading difficulty, blind spots, or changes in systemic health, such as major weight changes, kidney or liver disease. Early detection of toxicity is crucial to prevent irreversible blindness.
References