Living Life on the Fringes

Trey Trotter,* a 27-year-old man, visited our clinic for a routine eye exam. He had a history of myopia and had been a tobacco smoker for five years. When asked about visual and ocular issues, he said that he didn't have any concerns.

We Get a Look

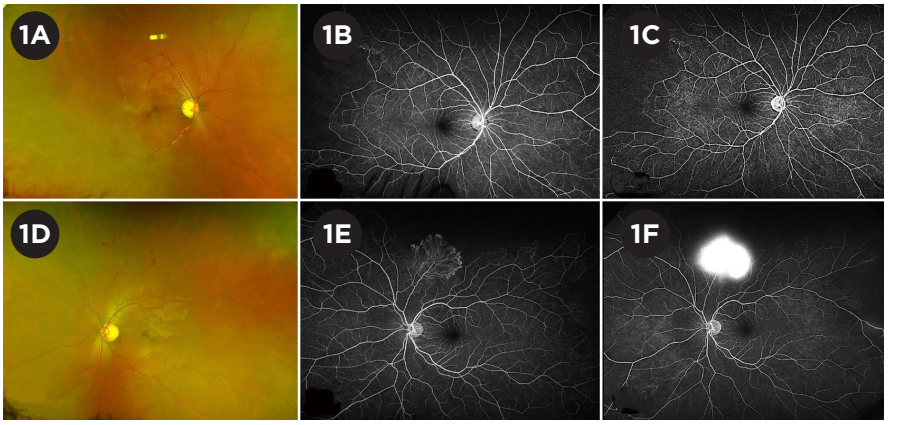
On examination, Mr. Trotter's vision corrected to 20/20 in each eye with a –0.25 D prescription. His IOP was 16 mm Hg in the right eye and 17 mm Hg in the left eye. There was no afferent pupillary defect; his ocular motility was intact; and his confrontation visual fields were full in both eyes.

On slit-lamp examination, the anterior segments were normal in both eyes.

The funduscopic exam in both eyes revealed pink and sharp optic nerves, with a cup-disc ratio of 0.6, and normal maculae. However, further inspection revealed arterial sheathing along the inferior arcade and sclerotic vessels in the temporal periphery of the right eye. In the left eye, a large area of retinal neovascularization was noted superiorly.

Spectral-domain (SD) macular OCT was normal in both eyes.

These findings prompted us to perform fluorescein angiography, which revealed peripheral temporal ischemia in both eyes and extensive leakage from the large peripheral retinal neovascular tuft in the left eye.



FUNDUS FINDINGS. *Right eye: (1A) Color fundus photograph shows sclerotic vessels temporally and arterial sheathing along the inferior arcade. Fluorescein angiography (FA) at (1B) 46 seconds and (1C) 13 minutes shows capillary dropout in the temporal periphery. The sheathed inferior artery does not stain or leak. Left eye: (1D) Color fundus photograph shows large area of neovascularization superiorly. (1E) FA at 31 seconds highlights the superior neovascular tuft with adjacent capillary dropout; (1F) diffuse leakage from the tuft is seen in the late frames at 9 minutes.*

Differential Diagnosis

The differential diagnosis for peripheral neovascularization and ischemia is a broad one. It includes the following conditions:

- diabetes,
- branch retinal vein occlusion,
- sickle cell retinopathy,
- hyperviscosity syndromes,
- retinal embolization,
- retinopathy of prematurity (ROP),
- familial exudative vitreoretinopathy,
- sarcoidosis,
- inflammatory diseases with retinal vasculitis,
- uveitis (including pars planitis),
- Eales disease,
- ocular ischemic syndrome, and
- incontinentia pigmenti.

Our Patient

Upon further questioning, Mr. Trotter reported a normal birth history, no intravenous drug use, and no family history of sickle cell disease or trait. However, he mentioned a history of rash for several years, and skin inspection revealed a discoid rash. We obtained a blood pressure reading, which was normal, and ordered a laboratory workup that included complete blood count, hemoglobin A1c, hemoglobin electrophoresis, and antinuclear antibody (ANA) panel.

All labs were normal with the exception of a positive ANA titer (1:320)

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that on reflex testing was positive for anti-Smith antibody.

Our Diagnosis

Based on the lab results, we considered that the etiology for our patient's peripheral ischemia with retinal neovascularization was lupus-associated vaso-occlusive retinopathy, which is an uncommon manifestation of systemic lupus erythematosus (SLE). Mr. Trotter was also diagnosed with discoid lupus erythematosus following a dermatology evaluation.

Discussion

Peripheral retinal neovascularization. Peripheral retinal neovascularization develops because of local retinal damage that causes ischemia. Common etiologies include systemic and retinal vascular conditions (e.g., sickle cell disease, retinal vein or artery occlusion, and ROP), inflammatory diseases with secondary retinal vasculitis (e.g., sarcoidosis, SLE, and uveitis), and congenital conditions (e.g., incontinentia pigmenti, retinitis pigmentosa, and familial exudative vitreoretinopathy). The workup of patients with peripheral retinal neovascularization should consist of a thorough medical history to identify a possible etiology, as well as tailored laboratory testing based on pertinent findings from the history and the ocular and physical exam.[1]

In our patient, the history of discoid rash, along with the negative review for other systemic conditions, pointed to the possible diagnosis of SLE. The laboratory evaluation confirmed the diagnosis.

Epidemiology. SLE is an autoimmune disease that affects mostly women of childbearing age, with a female to male ratio of 6:1 to 10:1. Black women have the highest incidence and prevalence.

Pathophysiology. The primary pathophysiology is aberrant overactivity of B cells, with resulting production of autoantibodies and activation of autoreactive T cells. The disease can affect any organ in the body.

Ocular involvement. Approximately one-third of patients with SLE have ocular involvement, with the most common manifestation being keratoconjunctivitis sicca.[2] Other ocular manifestations include episcleritis, scleritis, ischemic optic neuropathy, and choroidopathy.

Retinopathy has been reported in up to 29% of adults with SLE, and cotton-wool spots are the most common finding.[3] Occlusive retinopathy has been reported in approximately 3% to 11% of SLE patients with retinopathy. It is thought to represent immune complex–mediated vascular injury and microvascular thrombosis, characterized by widespread capillary nonperfusion of the retina.[4] This increases the chance of developing retinal neovascularization and vitreous hemorrhage.

Systemic SLE. A large prospective study in Canada found that 88% of patients with SLE-associated retinopathy had active systemic disease.[3] These patients had an overall lower survival rate due to active central nervous system involvement than did patients without retinopathy

Treatment. In cases of lupus retinopathy, it is important to control the SLE. Even in the absence of other systemic manifestations, patients with significant retinal findings require immunomodulatory therapy (IMT) to prevent vision loss.[2] Initial treatment is usually with oral corticosteroids, subsequently supplemented with or replaced by other immunosuppressive agents as part of a steroid-sparing strategy or for resistant disease.[2] Hydroxychloroquine is commonly used in conjunction with steroids. Other steroid-sparing therapies include azathioprine, cyclophosphamide, mycophenolate mofetil, methotrexate, cyclosporine, rituximab, and belimumab.

The mainstay of treatment consists of ablation of the retinal ischemic areas, as identified by fluorescein angiography. Scatter laser photocoagulation of the ischemic retina has been shown to cause regression of neovascular lesions by reducing angiogenic factors. Occasionally, anti-VEGF therapy has been used in an effort to prevent late-stage disease complications, such as vitreous hemorrhage or retinal detachments.

The Ophthalmologist's Role

Retinal lesions in SLE patients are of critical importance both visually and prognostically. It is important for the ophthalmologist to communicate with an internist or rheumatologist regarding the severity and activity of the patient's systemic disease.

Our patient was diagnosed with discoid lupus, but our exam clearly indicated manifestations of systemic lupus, which might necessitate further workup for SLE-related neurologic manifestations and more aggressive immunosuppression.

We offered Mr. Trotter panretinal photocoagulation to treat the areas of capillary nonperfusion. He declined the treatment and chose to be reevaluated in the eye clinic in four months.

*Patient name is fictitious.

1 Jampol LM et al. *Surv Ophthalmol.* 1994;38(6):519-40.
2 Dammacco R. *Clin Exp Med.* 2018;18(2):135-149.
3 Stafford-Brady FJ et al. *Arthritis Rheum.* 1988;31(9):1105-1110.
4 Jabs DA et al. *Arch Ophthalmol.* 1986;104(4):558-563.

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