MACULAR INFARCTION AS A PRESENTING SIGN OF SYSTEMIC LUPUS ERYTHEMATOSUS

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Purpose: We report two cases of macular infarction as a presenting sign of systemic lupus erythematosus (SLE).

Methods: Ophthalmic examination and intravenous fluorescein angiography were supplemented by rheumatology consultations and imaging.

Results: Two patients presented with complaints of decreased vision in one or both eyes. Systemic manifestations included fever, rash, and arthralgias, while serologic tests revealed an elevated erythrocyte sedimentation rate and positive antinuclear antibody titers in both cases, confirming the diagnosis of SLE in each case. Ophthalmoscopic changes included cotton-wool spots, intraretinal hemorrhages, and retinal edema. Fluorescein angiography revealed macular infarction with extensive retinal capillary nonperfusion in both patients.

Conclusion: Macular infarction is an uncommon but recognized complication of vasculitis associated with SLE. We report two additional cases of newly diagnosed SLE where vision loss secondary to macular infarction was the presenting sign of the disease. SLE should be considered in all patients who present with macular infarction. Visual prognosis is usually poor.


Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by the deposition of autoantibody immune complexes throughout the body. It is more commonly seen in women and blacks, with an incidence of 2 to 5 cases per 100,000 population per year in the United States.1

Ocular complications have been found in up to one third of patients with SLE.2,3 Previous articles have described such anterior segment findings as keratoconjunctivitis sicca,4 conjunctivitis, episcleritis, scleritis,5,6 interstitial keratitis, and iridocyclitis.7 SLE involvement of the posterior segment includes cotton-wool spots, intraretinal hemorrhages,5 retinal artery and/or vein occlusion,9 central serous chorioretinopathy,8 optic neuritis,10 and papilledema secondary to increased intracranial pressure.11 There have been few angiographically documented cases of macular nonperfusion in the setting of SLE (Table 1).12–17 In most patients with angiographic documentation, macular ischemia was the presenting sign of SLE.12,13,17

We report two cases of macular ischemia as the initial finding in SLE and review the literature. The collected cases support the view that macular ischemia can occur early in the course of SLE and that the visual prognosis tends to be poor.

Case Reports

Case 1

A 29-year-old Latina woman presented to the Manhattan Eye, Ear & Throat Hospital Emergency Department with a 2-week history of photopsias and progressive visual loss bilaterally. The patient also had arthralgias and headaches for 6 months and noted
intermittent rashes and fever over the last 2 years. Her medical history was significant for systemic hypertension.

At examination, the patient was afebrile, and blood pressure was 160/100 mmHg. Visual acuity was counting fingers in each eye. The pupils were reactive with no afferent papillary defect. Intraocular pressure and results of anterior segment examination were normal bilaterally. Posterior segment examination revealed trace vitreous cells, numerous sclerotic vessels, multiple cotton-wool spots, and scattered intraretinal hemorrhages in each eye (Fig. 1, A and B). Fluorescein angiography revealed extensive macular non-perfusion bilaterally (Fig. 1, C and D).

The patient was admitted to the hospital for evaluation. Laboratory testing revealed an erythrocyte sedimentation rate of 100 mm/h and an antinuclear antibody titer of 1:1,280 in a speckled pattern. Anticardiolipin antibody titers were negative. Magnetic resonance imaging of the brain without gadolinium revealed multiple punctate hyperintensities within the supratentorial white matter, consistent with cerebral vasculitis. The Rheumatology Department was consulted and made the diagnosis of SLE with both retinal and cerebral vasculitis. Solumedrol treatment was started intravenously, and the patient reported resolution of headache. Her disease was ultimately controlled with azathioprine therapy. Vision remained poor, however.

Case 2

A 31-year-old Indian Asian woman presented with loss of vision in the left eye for 10 days. She also reported fever, anorexia, and weight

<table>
<thead>
<tr>
<th>Case/Age (y)/Sex</th>
<th>Laterality</th>
<th>Fluorescein Angiography</th>
<th>Visual Acuity</th>
<th>Neovascularization</th>
<th>Initial Presentation</th>
<th>Benefit From Corticosteroids</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/29/F</td>
<td>OU</td>
<td>Capillary nonperfusion of the posterior pole bilaterally</td>
<td>OD: CF; OS: CF</td>
<td>No Vision loss OU</td>
<td>No</td>
<td>Current study, 2007</td>
<td></td>
</tr>
<tr>
<td>2/31/F</td>
<td>OU</td>
<td>Extensive capillary nonperfusion bilaterally</td>
<td>OD: 10/200; OS: 20/200</td>
<td>OD: no; OS: yes Vision loss OU</td>
<td>No</td>
<td>Current study, 2007</td>
<td></td>
</tr>
<tr>
<td>3/35/F</td>
<td>OS</td>
<td>Marked nonperfusion around the fovea</td>
<td>OS: CF</td>
<td>No Vision loss OS</td>
<td>Yes</td>
<td>Cooper et al, 2004</td>
<td></td>
</tr>
<tr>
<td>4/27/F</td>
<td>OU</td>
<td>Occlusion of the macular arterioles with macular ischemia bilaterally</td>
<td>OD: 1/20; OS: 1/20</td>
<td>No Vision loss OU</td>
<td>No</td>
<td>Sellami et al, 2002</td>
<td></td>
</tr>
<tr>
<td>5/30/M</td>
<td>OS</td>
<td>Occulsion of the macular arterioles with a severe macular filling defect</td>
<td>OD: 1/20</td>
<td>No Vision loss OS</td>
<td>Unknown</td>
<td>Sellami et al, 2002</td>
<td></td>
</tr>
<tr>
<td>6/37/F</td>
<td>OU</td>
<td>Extensive macular ischemia bilaterally</td>
<td>OD: 0.8; OS: 0.05</td>
<td>OU: Yes Unknown, but diagnosis made 13 y prior</td>
<td>No</td>
<td>Koch et al, 1992</td>
<td></td>
</tr>
<tr>
<td>7/38/F</td>
<td>OD</td>
<td>Extensive capillary nonperfusion, including the macula</td>
<td>CF</td>
<td>No Raynaud phenomenon</td>
<td>No</td>
<td>Jabs et al, 1986</td>
<td></td>
</tr>
<tr>
<td>8/24/M</td>
<td>OD</td>
<td>Extensive capillary nonperfusion, including the macula</td>
<td>3/400</td>
<td>No Unknown, but diagnosis made 2 y prior</td>
<td>No</td>
<td>Terhorst et al, 1983</td>
<td></td>
</tr>
<tr>
<td>9/39/F</td>
<td>OU</td>
<td>Nonperfusion of the macular capillary bed</td>
<td>OD: CF; OS: 20/200</td>
<td>OU: yes Loss of vision OU</td>
<td>Lost to follow-up</td>
<td>Gold et al, 1977</td>
<td></td>
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</table>

CF, counting fingers.

Table 1. Summary of Data on Reported Cases of Macular Nonperfusion in Systemic Lupus Erythematosus
loss over the last 3 months. Other systemic complaints included arthralgias, malar skin eruption, oral ulcers, dysacusis, and poliosis.

Best-corrected visual acuity was 20/200 in the right eye and 20/20 in the left eye. Results of external and anterior segment examinations were unremarkable. Posterior segment examination revealed trace vitreous cells and scattered sclerotic vessels with multiple cotton-wool spots and scattered intraretinal hemorrhages in each eye (Fig. 2, A and B). Fluorescein angiography revealed extensive macular nonperfusion bilaterally (Fig. 2, C and D).

Systemic evaluation revealed mucosal pallor and ulcerations and cyanotic extremities. The leukocyte count and hemoglobin level were both low at 4,000/mm³ and 4 mg%, respectively. The erythrocyte sedimentation rate was elevated at 104 mm/h, and the antinuclear antibody titer was positive (above the 1:320 cutoff for a positive test), confirming the diagnosis of SLE. Anticardiolipin antibody titers were negative.

Vision loss progressed to 10/200 in the right eye and 20/200 in the left eye over the next 2 months in spite of treatment with high-dose oral corticosteroids (60 mg/d). The oral corticosteroid dose was tapered, and systemic treatment with methotrexate (15 mg once a week) was started. She subsequently developed seizures and was referred for a neurologic workup.

Discussion

Macular infarction is an uncommon complication of SLE. However, with the addition of our patients, six of the nine patients had this finding as the initial manifestation of their disease (Table 1). Gold et al. described a woman with bilateral nonperfusion of the macular capillary bed who presented with vision loss and was subsequently diagnosed with SLE. Sellami et al. described two patients who presented with Purtscher-like retinopathy unrelated to trauma and were eventually diagnosed with SLE. Cooper et al. described a patient presenting with macular ischemia and a facial rash who ultimately developed SLE. The diagnosis of SLE was already established in only three of the cases of macular ischemia listed in Table 1. Furthermore, in only one of the nine patients with SLE-related macular ischemia did pulse corticosteroid treatment improve vision. Papadaki et al. described two patients with lupus retinal vasculitis and decreased vision, one of whom appeared to have widespread retinal capillary dropout on the published angiogram (although the researchers themselves did not refer to the findings as macular ischemia or infarction). Of note, both patients failed to respond to treatment with systemic corticosteroids and cyclophosphamide, but their conditions did improve after multiple rounds of plasmapheresis.

Beyond SLE, the differential diagnosis of macular...
ischemia is broad (Table 2). Gass\(^{19}\) was the first to describe various disorders that could lead to macular ischemia, including retinal artery and vein occlusions, systemic hypertension, diabetes mellitus, retinal telangiectasia, and radiation retinopathy. Since then, additional reports have implicated inflammatory diseases such as Behçet disease\(^{20–22}\) and sarcoidosis,\(^{20}\) infectious causes such as human immunodeficiency virus infection,\(^{23,24}\) thrombotic states such as sickle-cell disease\(^ {25,26}\) and thrombotic thrombocytopenic purpura,\(^ {27}\) and further iatrogenic causes such as aminoglycoside toxicity,\(^ {28,29}\) and transpupillary thermotherapy.\(^ {30}\)

Although overall systemic disease severity appears to be the greatest risk factor for the development of lupus-related retinopathy, the presence of anticardiolipin antibodies also appears to confer added risk for retinal vascular occlusion in patients with SLE.\(^ {31}\)

Moreover, recent reports have described elevated anticardiolipin antibody levels with retinal artery and vein occlusions and in the absence of SLE or conventional risk factors.\(^ {32–41}\) and it has been suggested that the presence of such autoantibodies can, irrespective of a diagnosis of SLE, lead to retinal vessel occlusion.\(^ {42}\) Although, to our knowledge, no histopathological studies have been reported on the eyes of patients with elevated anticardiolipin antibody levels in the absence of SLE, Nag and Wadhwa\(^ {43,44}\) examined the eyes of patients with SLE and suggested that occlusion results from immune complex–induced occlusion.

Table 2. Other Causes of Macular Infarction

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<th>Condition</th>
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<tr>
<td>Retinal artery occlusion(^ {19})</td>
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<tr>
<td>Retinal vein occlusion(^ {19,45})</td>
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<tr>
<td>Malignant hypertension(^ {19,46})</td>
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<tr>
<td>Diabetes mellitus(^ {19,47})</td>
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<tr>
<td>Retinal telangiectasia(^ {19})</td>
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<tr>
<td>Radiation retinopathy(^ {19,48})</td>
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<tr>
<td>Carotid artery occlusion(^ {19})</td>
</tr>
<tr>
<td>Posterior uveitis(^ {19})</td>
</tr>
<tr>
<td>Behçet disease(^ {20–22})</td>
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<tr>
<td>Sarcoidosis(^ {20})</td>
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<tr>
<td>Idiopathic retinal vasculitis(^ {20})</td>
</tr>
<tr>
<td>Acquired immunodeficiency syndrome(^ {23,24})</td>
</tr>
<tr>
<td>Thrombotic thrombocytopenic purpura(^ {27})</td>
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<tr>
<td>Transpupillary thermotherapy(^ {20})</td>
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<tr>
<td>Incontinentia pigmenti(^ {49})</td>
</tr>
<tr>
<td>Talc retinopathy(^ {30,51})</td>
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<tr>
<td>Sickle-cell retinopathy(^ {25,26})</td>
</tr>
<tr>
<td>Aminoglycoside toxicity, intravitreal and topical(^ {28,29})</td>
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<tr>
<td>Purtscher retinopathy(^ {52})</td>
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of small retinal vessels, which manifests clinically as cotton-wool spots.

In summary, we have reviewed the literature and reported two additional cases of macular ischemia presenting as the initial manifestation of SLE with no evidence of elevated anticardiolipin antibody titers. Although macular ischemia is an uncommon complication of SLE, when present it is often the initial sign of the disease, and visual prognosis tends to be poor, despite the use of high-dose systemic corticosteroids and noncorticosteroid immunosuppressive agents.

Key words: ischemia, occlusion, vasculitis.

References
24. Kalogeropoulos CD, Spyrou P, Stefanis D, et al. Anti-