Bilateral Optic Neuritis as First Manifestation of Systemic Lupus Erythematosus

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A 21-year-old woman presented with bilateral optic neuritis, combined with central retinal vein occlusion. General physical examination and neurologic consultation revealed no other findings. Laboratory investigation yielded an elevated erythrocyte sedimentation rate, positive LE preparation, elevated ANA titer, and elevated blood urea nitrogen and creatinine levels. Diagnosis of systemic lupus erythematosus (SLE) was made. Renal failure developed quickly and she was treated with hemodialysis, transfusion and subsequently systemic corticosteroid. Anti-phospholipid antibody was positive to lupus anti-coagulant and the titer was normalized after 2-month steroid therapy at which time the visual outcome differed between the eyes. The right eye showed improvement in visual acuity and visual field, but the left eye was not improved and retained a central scotoma. SLE needs to be considered in young women with optic neuritis when other causes of optic neuritis have been excluded, and serologic tests including anti-phospholipid antibody should be conducted.

Key words: central retinal vein occlusion, optic neuritis, systemic lupus erythematosus

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic, systemic, immunologically mediated disease of unknown etiology. The main ocular manifestations of SLE include lesion of the retinal vasculature, eyelid skin and neuro-ophthalmic pathways. However, ocular manifestations have not been included in the diagnostic scoring system for establishing the clinical diagnosis of SLE. (Table 1) Retinal vascular abnormalities are the most common intraocular expression of SLE. The retinopathies include nerve-fiber layer infarct (cotton-wool spot) and hemorrhage. Cases of severe retinal vaso-occlusive disease such as central retinal artery occlusion (CRAO), central retinal vein occlusion (CRVO), and branch retinal artery occlusion (BRAO) in SLE in association with the lupus anticoagulant have been reported, and the retinal disease is thought to be related to this autoantibody. Although a variety of ophthalmic manifestations may be seen in SLE, involvement of the optic nerve in the course of this autoimmune disease is rare. Gold and associates, in reviewing 9 series involving 1,372 patients diagnosed with SLE, found reports of ‘papilledema’ in 13 patients and ‘optic atrophy’ in only one. In a report in the neurologic literature, optic neuritis was

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thought to be the presenting sign in 3 young females who ultimately were shown to have SLE.5

The current report presents a 21-year-old woman with bilateral optic neuritis and CRVO as the only signs of clinical disease who manifested diagnostic evidence of SLE upon further evaluation and showed different prognosis in both eyes.

CASE REPORT

A 21-year-old woman presented to the eye clinic with a 2-day history of visual disturbance in both eyes. Her family history and past history were unremarkable. Current and past medications included a daily multivitamin. She had no skin abnormalities and blood pressure was 130/80 mmHg.

Ocular examination revealed best-corrected vision of counting fingers in both eyes. The pupils were moderately dilated and did not react to direct or consensual light. The intraocular pressure was 16 mmHg in both eyes. Ocular movements were normal. The anterior segments and media were normal bilaterally. Ophthalmoscopy revealed mild hyperemia of both optic nerve heads. The margins of both optic discs were mildly blurred, and there were multiple large cotton wool spots and flame-shaped hemorrhages in both eyes. (Fig. 1) Fluorescein angiography revealed leakage of dye around both optic discs, a nonperfusion area corresponding with cotton-wool spots, and tortuosity of retinal veins in both eyes. (Fig. 2) Humphrey automated perimetry revealed decreased sensitivity over almost the entire fundus in both eyes. Furthermore, visual field of the left eye revealed deep and localized scotoma closed to fixation. Visual evoked potential revealed a mild reduction of amplitude and increased latency in both eyes.

Physical examination and neurologic consultation were normal. She underwent computed tomography as well as magnetic resonance imaging of the brain, in search of lesions suggestive of multiple sclerosis. No demyelinating lesion was found in the brain. Routine laboratory study showed: white blood cells 8.9 \times 10^{3}/\text{mm}^3 (normal value 4.5-11.0 \times 10^{3}/\text{mm}^3) with normal differential count, hemoglobin 8.8 g/dl (normal value 12-15 g/dl), platelets 21.9 \times 10^{3}/\text{mm}^3 (normal value 130-400 \times 10^{3}/\text{mm}^3), erythrocyte sedimentation rate 56 mm/h (normal value 0-30 mm/h), C-reactive protein 9.5 (normal value 0.1-0.8), prothrombin time 11.3 seconds (normal value < 13 seconds), an partial thromboplastin time 23.3 seconds (normal value < 26 seconds), blood urea nitrogen 72 (normal value 5-23), and serum creatinine 2.8 (normal value 0.6-1.2). Urinalysis revealed proteinuria (2.4 g/dl). The patient, tentatively diagnosed with
lupus optic neuritis combined with CRVO and lupus nephritis, was admitted to the nephrologic department. Oliguric renal failure and thrombocytopenia quickly progressed and treatment was started with hemodialysis and blood component transfusion. Three days later, extensive laboratory studies revealed decreased C3/C4 level, positive Anti-ds DNA, positive LE cell, positive anti-nuclear antibody, negative rheumatoid factor, negative anti-cardiolipin antibody, and positive lupus anti-coagulant. She also manifested malar rash and arthritis in three peripheral joints. Renal biopsy was performed and suggested lupus nephritis. She was diagnosed as having SLE on the basis of fulfilling 5 of the 11 criteria for such diagnosis: malar rash, arthritis, renal disorder, hematologic disorder, and positive antinuclear antibody.

High-dose immunosuppressive therapy was started with a corticosteroid (prednisone, 80 mg/d for 2 weeks tapering to a maintenance dosage of 5 mg/d
over 6 weeks.) There was no improvement in visual acuity before the commencement of steroid therapy. After three weeks of therapy, the patient’s visual acuity had improved to about 20/200 in her right eye but still remained in the counting fingers range in her left eye. On fundus examination, the blurring of optic disc margins was improved and the cotton wool spots and flame-shaped hemorrhage were also decreased. After 2 months of therapy, her visual acuity of the right eye was improved to 120/200, but the left eye remained in the counting fingers range. The fundus was much improved in both eyes, but cotton-wool spots and retinal hemorrhage still remained. (Fig. 3) Automated perimetry revealed a large central scotoma in the left eye. (Fig. 4) The titer of anti-cardiolipin antibodies was normalized

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**Fig. 4.** After 2 months of therapy, automated perimetry shows a large central scotoma in the left eye.
Table 1. 1982 revised criteria of the American Rheumatism Association for the diagnosis of systemic lupus erythematosus

- Malar rash
- Discoid rash
- Photosensitivity
- Oral ulcers
- Arthritis in two or more peripheral joints
- Serositis (pleuritis or pericarditis)
- Renal disorder (proteinuria or urinary casts)
- Neurologic disorder (seizures or psychosis)
- Hematologic disorder (Positive LE-cell preparation, presence of anti-DNA or anti-Sm antibody, or false-positive VDRL)
- Presence of antinuclear antibody

A diagnosis of SLE is made if at least 4 of the 11 revised criteria are present.

after 2 months of therapy.

DISCUSSION

Nowadays, a diagnosis of SLE is made if at least 4 of the 11 revised criteria established by the American Rheumatism Association are present, serially or simultaneously, during any interval of observation. Although none of these criteria include ocular findings, it is notable that in two surveys 29% of hospitalized patients and 8% of outpatients with SLE experienced ocular vaso-occlusive changes attributed to their systemic disease.

Our patient fulfilled 5 of the 11 criteria for the diagnosis of SLE, but her initial manifestation was simultaneous bilateral optic neuritis combined with CRVO. In a study of neuropsychiatric manifestations of SLE, Feinglass et al. noted that one of 140 SLE patients suffered an optic neuropathy, giving an estimated prevalence of 0.7%. Jabs and colleagues reported seven patients with optic neuropathy in association with SLE, although none of these patients had presented with optic neuropathy as the initial manifestation. In 1978, Cinefro RJ et al. reported a 57-year-old white man presenting with unilateral optic neuritis. In Korea, In Taek Kim et al. reported a case of bilateral papilledema in an 18-year-old female with cerebral venous thrombosis and SLE. They also reported three cases of CRVO, BRVO and BRAO in association with SLE. Other CNS lesions have been commonly associated with optic neuritis. In a previous study, spinal cord disease was the most commonly associated CNS lesion, being reported in 13 (54%) of 24 cases.

The pathogenesis of optic neuritis is still unclear. Asherson et al. concluded that milder cases of optic neuritis, characterized by demyelination, could be due to a less severe ischemia. Conversely, more severe and irreversible cases, characterized by axonal necrosis, could be due to a much more severe ischemia. It is clear from cases described in the literature as well as our own and like our case, that bilateral optic neuritis appears to occur more frequently than monolateral optic neuropathy.

Retinal involvement in SLE is quite common. Eight-eight percent of patients with lupus retinopathy had active systemic disease in a prospective clinical study, and SLE patients with retinopathy had significantly decreased survival compared with SLE patients without retinopathy. Severe visual loss does not usually occur in patients with lupus retinopathy. In a study by Stafford-Brady et al., 38% of patients with retinopathy had lupus anticoagulant in contrast with only 17% of unselected SLE patients from the same lupus clinic. Recently Asherson et al. have suggested that antiphospholipid antibodies represent a risk factor for the development of ocular vascular disease in SLE patients. Anti-cardiolipin antibodies have been associated with various manifestations of SLE. Especially, the IgG isotype of anti-cardiolipin antibodies is considered more specific and pathogenic. Oppenheimer and Hoffbrand reported an association of optic neuritis with anticardiolipin antibodies and lupus anticoagulant. Our patient tested positive for lupus anticoagulant, but negative for anticardiolipin antibodies.

The known standard treatment for lupus optic neuritis includes intravenous methylprednisolone (1 g/day/3 days) and oral corticosteroid (1 mg/kg/day). Galindo-Rodriguez et al. reported that nearly one-third (10 of 35) were refractory to corticosteroid or oral immunosuppressants. In another study, cyclophosphamide therapy demonstrated a successful effect on lupus optic neuritis refractory to corticosteroid or oral immunosuppressants, but the study was a non-randomized and non-controlled trial.
Our patient was treated with boluses of methylprednisolone and oral corticosteroid. The visual acuity of the right eye was improved after 3 weeks of therapy, but that of the left eye was not improved. After 2 months of therapy, the right eye visual acuity was much improved, but the left eye remained in the counting fingers range. Automated perimetry revealed a large central scotoma in the left eye. The visual outcome in the cases reported in the literature has often been poor; visual acuity was 20/200 or worse in 13 of the 21 cases.

In summary, we report one unusual case of optic neuritis associated with SLE. She had simultaneous bilateral optic neuritis combined with CRVO as the initial manifestation of SLE. The results of serologic study were positive to lupus anticoagulant and the titer was normalized after 2-month steroid therapy. Compression of the central retinal vein by the swollen optic nerve could have predisposed the vein to CRVO. After steroid treatment, the visual outcome differed between the eyes. Visual acuity and field improved in the right eye, but not in the left eye which retained a central scotoma. SLE needs to be considered in young women with bilateral optic neuritis when other causes of optic neuritis have been excluded, and serologic tests including antiphospholipid antibody should be conducted.

REFERENCES