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Case Report	: Atypical Optic Neuritis as An Initial Manifestation of Systemic Lupus Erythematosus: A Case Report
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Atypical Optic Neuritis as An Initial Manifestation of Systemic Lupus Erythematosus: A Case Report

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Abstract

Introduction: One of the uncommon manifestations of systemic lupus erythematosus (SLE) is optic neuritis. It can be an early sign of or a risk factor for autoimmune diseases. The incidence of SLE is 1 to 10 per 100,000 with only less than 1% of optic nerve involvement.

Purpose: To report a case of systemic lupus erythematosus with an initial manifestation of atypical optic neuritis.

Case report: We report a case of a 30-year-old woman who came with a chief complaint of painless and progressive vision loss in both eyes 2 weeks ago. Vision loss is preceded by fever, cough, and flu-like symptoms several days before. History of autoimmune disease is unknown. Visual acuity in both eyes was 2/60. Color vision and contrast sensitivity of both eyes were decreased. Central and cecocentral scotomas were found as visual field defects in both eyes. Both pupils have decreased direct and indirect light reflexes. Funduscopic examination of both eyes showed optic disc swelling with obscuration of the optic nerve head margins, AV ratio 1:3, AV crossing, soft exudates, hard exudates, dot hemorrhages and intraretinal hemorrhages. Laboratory examination found the ANA test result was reactive. Patient was diagnosed with Atypical Optic Neuritis and Retinopathy Suspected caused by SLE of both eyes and Hypertension. Patient was hospitalized for 3 days and given methylprednisolone IV 1000 mg/day. At the follow-up visit 1 week after hospitalization, there were improvements in visual acuity, color vision, contrast and amsler grid examination.

Conclusions: Neuro-ophthalmic manifestations of SLE are rare, but they can be the initial manifestation of active SLE. The most common neuro-ophthalmic manifestation of SLE is optic neuritis. SLE-associated optic neuritis has variable response after treatment, depending on the degree of axonal loss. Early treatment is very crucial for better visual outcomes.

Keywords: ***atypical optic neuritis, systemic lupus erythematous, autoimmune disorder***

I. Introduction

Optic neuritis (ON) refers to an acute disease with focal inflammation of the optic nerve. It can be associated with demyelination, infectious disease, neurologic and systemic inflammation or autoimmune disease. It may affect any portion of the

optic nerve, one or both optic nerves. Based on a previous study, the incidence of optic neuritis ranges from 0.83-5.36 per 100.000 populations. In Central Europe, the incidence of optic neuritis is 5 cases per 100.000 persons per year with the mean age at onset is 36 years. Most of the patients, about 70% are women. The clinical features of ON can be classified as typical ON and atypical ON. A typical ON is a specific clinical pattern associated with demyelinating lesion which can be idiopathic, isolated and associated with multiple sclerosis (MS). An atypical ON is caused by any other disease and not related to MS. It can be classified into those without systemic disease including neuromyelitis optica spectrum disease (NMOSD), myelin oligodendrocyte glycoprotein (MOG) ON, and chronic relapsing inflammatory optic neuropathy (CRION), and those with systemic disease includes infectious and autoimmune causes such as myasthenia gravis (MG), rheumatoid arthritis (RA), ankylosing spondylitis (AS), and systemic lupus erythematosus (SLE).[1–3]

Systemic lupus erythematosus (SLE) is a chronic autoimmune inflammatory disease that affects several organ systems. The prevalence of SLE ranges from 72.8 to 178 cases per 100.000 patients per year. It occurs frequently in African and Asian populations, with the median age of onset in the late teens to early 40s. It commonly occurs in women, which are 9 times more susceptible than men. Central nervous system (CNS) involvement occurs in 20%-60% of the cases, whereas only 1% of optic nerve involvement in SLE. Neuro-ophthalmic manifestations are rare, but the most common is optic neuritis. The prevalence of SLE-associated ON is 0.6%-1%, and it can be the initial manifestation of SLE. It is very important to the ophthalmologist to differentiate between SLE-associated ON and idiopathic ON due to poorer visual impairment and stronger dependency of treatment.[3–6] This case report aims to describe atypical optic neuritis as an initial manifestation of systemic lupus erythematosus.

II. Case Report

A 30-year-old woman came with a chief complaint of painless and progressive vision loss in both eyes 2 weeks ago. The vision loss initially started in the left eye

and then followed by the right eye. Patient also complained of fever, cough, and flu-like symptoms 10 days before. Patient used corticosteroid and antibiotic eye drops that purchased by herself to relieve the complaints, but there was no improvement. Patient had no history of recurrent eye redness, periocular pain, and gaze-evoked pain. Patient denied any history of scalp tenderness, jaw claudication, nausea, vomiting, headache, seizures, muscular weakness, and unconsciousness. There was no history of shortness of breath, frequent choking during sleep, palpitations, numbness and tingling. Patient had no history of surgery, trauma and spectacle use. She also had no history of systemic diseases such as hypertension, diabetes mellitus, high cholesterol, cardiovascular disease, allergies, asthma, thyroid disease, and tuberculosis. Patient had never done an autoimmune disease examination before. History of tobacco smoking or drinking alcohol is denied. There was no history of the same complaint in the family.

General examination was within normal limits with a body mass index of 28.8 which indicated obesity. The blood pressure was 180/120 mmHg. Ophthalmology examination showed orthotropic in the primary position, normal eye movement in all gaze directions. Visual acuity in both eyes was 2/60, with normal intraocular pressure in both eyes.

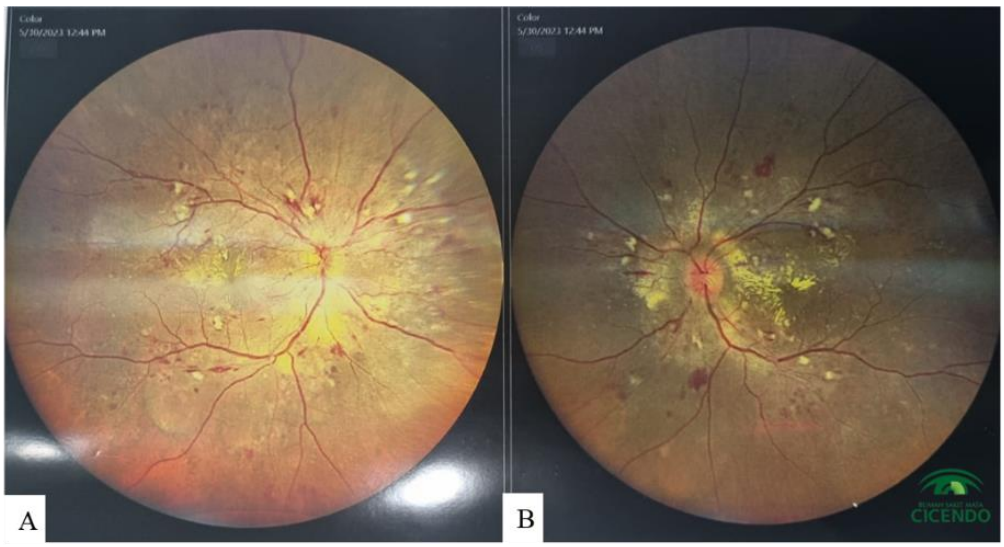

Figure 2.1. Funduscopic examination of the right eye (A) and left eye (B) showed both eyes had optic disc swelling with obscuration of the optic nerve head margins, AV ratio 1:3, AV crossing, soft exudates, hard exudates, dot hemorrhages and intraretinal hemorrhages.

Anterior segment examination showed both pupils have decreased direct, indirect light reflexes and relative afferent pupillary defect (RAPD) were difficult to assess. Funduscopic examination showed both eyes had optic disc swelling with obscuration of the optic nerve head margins, AV ratio 1:3, AV crossing, soft exudates, hard exudates, dot hemorrhages and intraretinal hemorrhages (Figure 2.1).

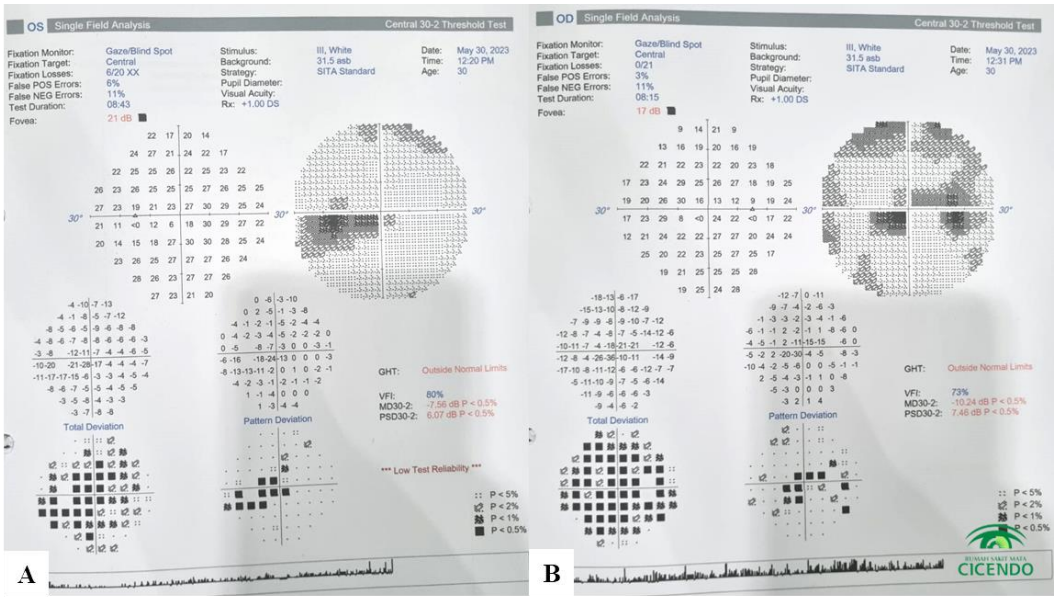

Figure 2.2. Automated perimetry of the left eye (A) and the right eye (B) showed central and cecocentral scotoma.

Color vision examination with Ishihara color testing, revealed demoplate in the right eye and 15/21 in the left eye. Amsler grid examination revealed a central scotoma in both eyes. There was a decrease in contrast sensitivity in the right eye to 5% and 2.5% in the left eye. Examination of other cranial nerves was within normal limits, no neurological deficit was found and motoric examination in all extremities was within normal limits. Visual field examination with automated perimetry revealed a central and cecocentral scotomas in both eyes (Figure 2.2). Optical coherence tomography (OCT) of both optic nerves showed bilateral optic disc swelling with increased retinal nerve fiber layer (RNFL) thickness in both eyes (Figure 2.3). Macular OCT examination of both eyes showed hyporeflective

intraretinal and outer retinal structures, and disrupted foveal depression with subretinal fluid in the outer layer suggesting a macular edema.

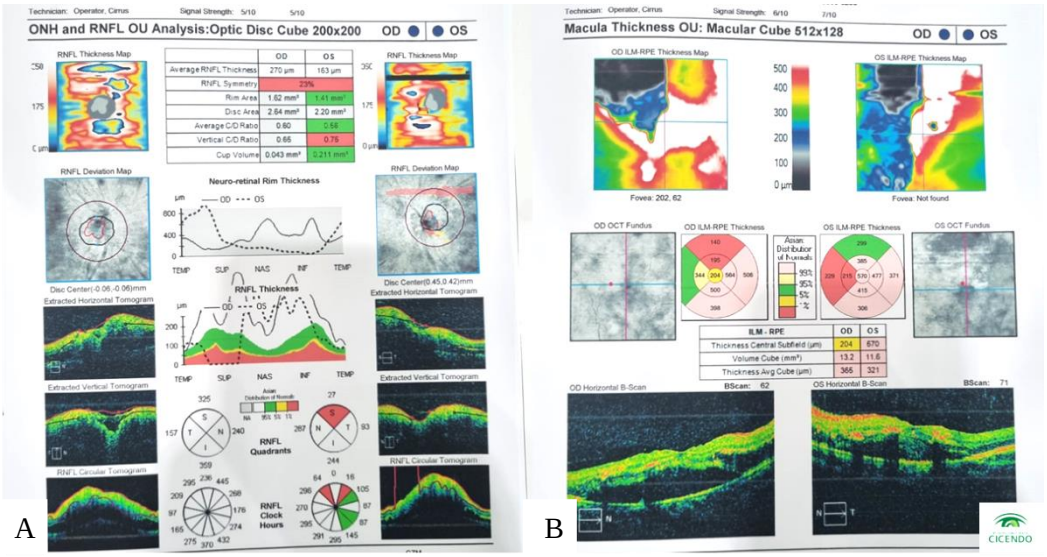

Figure 2.3 Optical coherence tomography (OCT) of optic nerves (A) showed bilateral optic disc swelling with increase RNFL thickness. OCT of macula (B) of both eyes showed hyporeflective intraretinal and outer retinal structures, and disrupted foveal depression with subretinal fluid in the outer layer suggesting a macular edema.

The patient was diagnosed with Atypical Optic Neuritis and Retinopathy Suspected caused by Autoimmune Disease dd/ Infection dd/ Hypertensive Retinopathy Grade IV of both eyes. Patient was hospitalized for 3 days to receive methylprednisolone intravenous (IV) of 1000 mg per day for 12 times, followed by oral methylprednisolone 1mg/ kg body weight per day, omeprazole IV 40 mg once a day, mecobalamin IV 500 mcg once a day, and oral D3 vitamin 400 IU twice a day. Patient then underwent laboratory tests including IgG and IgM of toxoplasma, cytomegalovirus, HIV test, ANA test and Rheumatoid Factor examination. Patient was consulted to Internal Medicine unit for treatment of hypertension and treated with bisoprolol 2.5 mg once a day, candesartan 16 mg once a day, and amlodipine 10 mg once a day. Patient was permitted to continue methylprednisolone injection if blood pressure was under 190/100 mmHg. Patient was consulted to Vitreoretina unit and the treatments were continued.

On the first day of admission, patient felt an improvement of her vision. The visual acuity was 0.32 in the right eye and 0.25 in the left eye. On the second day of admission, ishihara examination of both eyes showed improvement with 10/21 in the right eye and 15/21 in the left eye. On the third day of admission, visual acuity was 0.4 in the right eye and 0.32 in the left eye. Ishihara examination showed 15/21 in the right eye and 18/21 in the left eye. Amsler grid examination was within normal limits. There was an increase in contrast sensitivity examination with 2.5% in the right eye and 1.25% in the left eye. After 12 injections of methylprednisolone IV, patient was given oral methylprednisolone 64 mg once a day, lansoprazole 30 mg once a day, mecobalamin 500 mcg once a day, and D3 vitamins 400 IU twice a day.

The patient was followed up 1 week after hospitalization. Patient felt an improvement of the visual acuity. Patient came with laboratory result of non-reactive HIV, reactive IgG CMV and reactive ANA test. The vital sign showed normal blood pressure of 120/80 mmHg. Visual acuity was 0.32 in the right eye and 0.25 in the left eye. Patient was diagnosed with Atypical Optic Neuritis and Retinopathy Suspected caused by SLE of both eyes and Hypertension. Patient's treatment was continued with oral methylprednisolone tapering off with 56 mg one a day and other medications were continued. Patient was advised to examine the ANA profile. Patient was also consulted to Internal Medicine unit and given nutritional vitamins three times a day, pregabalin 75 mg once a day, and continue hypertension medications. Prognosis in this case varies, depending on the disease's severity, response to treatment, and patient's compliance.

III. Discussion

Systemic lupus erythematosus (SLE) is a chronic autoimmune inflammatory disease which can affect multiple organ systems. The incidence of SLE is 1 to 10 per 100,000 person-years with a prevalence of 20-200 per 100,000 person-years. The incidence of SLE is higher in Asian, African, and Hispanic populations. The median age of onset is late teens to early 40s. It mainly affects women of childbearing age. which are 9 times more susceptible than men. Neuro-ophthalmic

manifestations of SLE are rare, with a prevalence of 3.6%. The most common manifestation which can be the initial presentation of active SLE or along the course of the disease is optic neuritis. SLE-associated optic neuritis (ON) is uncommon, only 0.6%-1%. Optic neuritis is the most common clinically isolated syndrome in neuro-ophthalmic manifestation of SLE. Lin et al. reported that only 50% of SLE-associated ON patients recovered visual acuity to better than 20/25.[2,3,5,7] In this case, a 30-year-old woman in a productive or childbearing age presented with painless and progressive vision loss in both eyes preceded by fever, cough, and flu-like symptoms 10 days before. Patient had no other symptoms. Patient was diagnosed with Atypical Optic Neuritis and Retinopathy Suspected caused by SLE of both eyes with Hypertension, as the ANA test result came as positive. This case was one of the rare neuro-ophthalmic manifestation of SLE, as the initial manifestation in this case was atypical optic neuritis.

Symptoms due to SLE are caused by the formation of multiple autoantibodies, deposition of immune complexes in multiple organs, complement activation and stimulating mediators of inflammation. It is believed that T-cells dysregulation is triggered in the acute phase by inflammation that causes axon demyelinating injury. This condition resulted in increased autoimmune B cells' response against self-antigens in tissue or organs. Demyelinating symptoms may be the first manifestation of SLE, as a clinically isolated syndrome, before the appearance of other typical features of the disease. This is similar to our case report that the patient's first clinical manifestations present as a clinically isolated syndrome of SLE without any systemic symptoms. Patient had no history of other systemic diseases except for hypertension which was found out at this time, because of the patient did not routinely check or controlled for her blood pressure. Patient also had no history of diseases or symptoms related to multiorgan system involvement. Demyelinating symptoms of atypical optic neuritis of both eyes, in this case, was proof of axonal injury caused by SLE.[3,5,8,9]

Several studies reported a wide range of signs and symptoms related to SLE-associated ON. At first, it can be presented as progressive painless visual loss unilaterally or bilaterally, with or without periocular pain in the early stage. Then

proceed with positive RAPD if unilateral, reduced color vision, reduced contrast sensitivity, photophobia, visual field defect with funduscopic evaluation revealed optic disc edema, severe hemorrhages and exudates, vitritis, and neuroretinitis. Other manifestations of SLE include scleritis, episcleritis, retinitis, and uveitis. The retinal disease affects around 3%-29% of patients with SLE. Lupus retinopathy is associated with more severe form of the disease and has a poor prognosis. Lupus retinopathy detected by fundus examination, correlates well with SLE disease activity. Its pathophysiology is complex and involves immune complex depositions in retinal vessel walls leading to vasculitis and microinfarct of retinal vessel walls, autoantibody-mediated neuronal cell damage, inflammatory and thrombotic microangiopathy and disruption of the blood–brain barrier. This microenvironment leads to mitochondrial damage, resulting in a reduction in synaptic activity and neuronal death. The most common ocular findings in Lupus retinopathy are soft exudates or cotton wool spots, hard exudates, dot hemorrhages, arteriolar and venular narrowing, vasculitis and central retinal or vein occlusions. In more severe form, ocular findings include neovascularization, retinal detachment and vitreous hemorrhages.[3,5,7,10,11] In this case, our patient also had the symptoms of progressive painless visual loss, visual field defect of both eyes with central and cecocentral scotomas, reduced color vision and contrast sensitivity. Both pupils have decreased direct, indirect light reflex and RAPD were difficult to assess because of both eyes were affected. Funduscopic examination of both eyes in this case revealed an optic disc swelling with obscuration of the optic nerve head margins, AV ratio 1:3, AV crossing, soft exudates, hard exudates, dot hemorrhages and intraretinal hemorrhages. These findings suggesting that patient also has Lupus retinopathy on both eyes.

Visual field examination of SLE-associated ON may show central scotoma, cecocentral scotoma, arcuate defects or even generalized depression in functional visual loss. This pattern similar to our patient in this case which showed central and cecocentral scotomas in both eyes. Optical coherence tomography (OCT) is a safe and objective method with non-invasive imaging technology, that permits high resolutions cross-sectional pictures of the retinal layers. OCT is able to detect

thinning of retinal nerve fiber layer and macula that useful for a biomarker in neurodegenerative diseases, such as SLE. Based on several studies, there is a significant decrease or degenerative thinning of the peripapillary retinal nerve fibre layer (pRNFL), central foveal flattening, epiretinal membrane and thinning of macular photoreceptor layer in patients with SLE. Peripapillary RNFL thinning especially on temporal sectors is a proven biomarker of neurodegeneration diseases. Our patient also has abnormality findings on OCT of both optic nerve that showed bilateral optic disc swelling with increase RNFL thickness in both eyes. These findings indicate that patient still in acute phase, which later can cause thinning in pRNFL thickness along with the development of optic atrophy after 4-8 weeks. OCT changes significantly correlates with steroid intake duration of more than 3 months and progression of SLE disease activity. Photoreceptors are the most energy-demanding neurons, mitochondrial damage and disturbance neuron-glia metabolic coupling cause reduction in macular photoreceptor layer.[7,12,13] Based on macular OCT both eyes showed hyporeflective intraretinal and outer retinal structures, disrupted foveal depression with subretinal fluid in outer layer suggested a macular edema.

Atypical optical neuritis often carries a significant risk of autoimmune diseases including myasthenia gravis (MG), rheumatoid arthritis (RA), SLE, and ankylosing spondylitis (AS), for which optic neuritis may be an early sign or independent risk factor for autoimmune diseases. In addition, patients with optic neuritis under 65 years or those who are young and female were susceptible to optic neuritis-associated autoimmune disease, with a prevalence of 55%–70%. The pathogenesis of SLE-associated ON is due to vasculitis or thrombotic vaso-occlusive phenomenon involving small arterioles, leading to axonal necrosis and permanent damage of the optic nerve. This process causes poor visual outcomes in cases of SLE-associated ON.[3,5,7]

The severity of SLE depends on the organs involved in the immune processes. It may be difficult to diagnose because early signs and symptoms are not specific. The complex clinical presentation and pathogenesis of SLE make it difficult to define. Various autoantibodies, such as anti-double-stranded DNA, anti-Ro, La,

Sm, nucleosome, N-methyl-D-aspartate receptor, and phospholipid, have been identified to cause SLE. Classification criteria are essential for identification. European Alliance of Associations for Rheumatology/American College of Rheumatology (EULAR/ACR) in 2019, classified SLE based on positive ANA test as an obligatory criterion in addition to seven clinical criteria with three immunological domains. These criteria have excellent performance, strong operating characteristics, with excellent sensitivity and specificity.[4,14,15] In this case, the patient already include in the entry criterion with reactive ANA test, another test of immunological domains and long-term observation for any clinical involvements are needed to classify and apply the additive criteria to the patient.

Appropriate early treatment with high-dose corticosteroid is necessary to achieve maximum clinical improvement of SLE-associated optic neuritis or neuropathy. Active SLE has a rapid clinical response to intravenous corticosteroid treatment, but visual outcome after the treatment has variable responses. Visual outcomes depend on the degree of axonal necrosis and axonal loss. Recommendation treatment for SLE optic neuritis is high-dose intravenous methylprednisolone (1000 mg/day for three days) followed by oral prednisone (1 mg/kg/day) as the first line of treatment. In case of relapsing or multiple episodes of optic neuritis or other disease related to SLE, requires long-term immunosuppressive treatment such as cyclophosphamide, cyclosporine, methotrexate, and azathioprine. The complication of delayed or no treatment was a degradation of visual function. The previous study stated that early initiation of intravenous cyclophosphamide with methylprednisolone is the best treatment option for neuro-ophthalmic manifestations of SLE that might prevent vision loss. SLE-associated with retinal vasculopathy has better outcomes with anticoagulation, while retinal microangiopathy with immunosuppressive agents.[4,5,10,14] In this case, the patient had received 12 doses of methylprednisolone IV of 1000 mg per day, followed by oral methylprednisolone 1mg/ kg body weight per day, omeprazole IV 40 mg once a day, mecobalamin IV 500 mcg once a day, and oral D3 vitamin 400 IU twice a day.

A good history taking and thorough physical examination are essential for making a proper diagnosis. Timely identification of the disease and early treatment has an excellent prognosis. Proper diagnosis and prompt treatment with high-dose corticosteroids promote good visual outcomes, but SLE has a variable response to visual outcomes after treatment. Prognosis and visual outcomes are not quite good as that in inflammatory demyelinating optic neuritis, because occlusive vasculitis cause secondary demyelination and axonal necrosis leading to axonal loss thereby affecting the visual outcomes. Based on these conditions, early treatment is very crucial for better visual outcomes and has an excellent prognosis.[4,5,14]

IV. Conclusion

Neuro-ophthalmic manifestations of SLE are rare. SLE-associated optic neuritis can be the initial presentation of active SLE. Symptoms due to SLE are caused by complex dysregulation of the immune system affecting multiple organs of the human body. Visual outcomes of SLE-associated ON have variable responses and depend on the degree of axonal loss. Early diagnosis and treatment with high-dose corticosteroids promote better visual outcomes.

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