

A Case of Isolated Oculomotor Nerve Palsy in Systemic Lupus Erythematosus

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A 47-year-old woman with a history of systemic lupus erythematosus (SLE) presented for neurologic evaluation due to diplopia and ptosis that she had noted upon awakening 2 days earlier. Physical examination demonstrated the left eye to be deviated downward and laterally, with a nonreactive pupil; the right eye and the remainder of the cranial nerves tested normally.

The patient confirmed having headache and fatigue but denied having facial numbness, dysphagia, dysarthria, sunlight sensitivity, hypertension, or kidney involvement. She was not on any medications for SLE—she had stopped taking hydroxychloroquine therapy 2 years previously because of her concern that it may cause retinopathy. Her disease appeared to be in remission, because her symptoms prior to this episode had been mild. However, she had not been regularly seeing a rheumatologist or other clinicians. Her previous symptoms of SLE had included cutaneous manifestations, mild arthralgias, hair loss, oral ulcers, headache, fatigue, and pleurisy.

Upon admission, computed tomography angiography (CTA) and magnetic resonance angiography scans showed no significant abnormalities. Antinuclear antigen (ANA) test results were positive, with low titer anti-double-stranded DNA antibodies and a low C4 level with 1+ proteinuria consistent with her SLE history. Treatment with high-dose intravenous pulse corticosteroids (prednisone) and a taper of oral corticosteroids was initiated, resulting in noticeable improvement in 2 days, although the pupillary dilation and ptosis continued. After 5 days with

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partial improvement, she was discharged on oral corticosteroids and hydroxychloroquine therapy and was scheduled for outpatient follow-up with a rheumatologist for further management of symptoms.

DISCUSSION

SLE is prevalent worldwide, with a highest reported prevalence rate of 241 per 100,000 people and a highest reported incidence rate of 23.2 per 100,000 person-years.¹ This systemic autoimmune disease predominantly affects women of childbearing age. While the pathophysiologic mechanism of SLE is not fully understood, the prevailing hypothesis involves a multifactorial pathogenesis involving a genetic predisposition to the production of autoantibodies to nucleic acids that requires an environmental trigger to initiate pathogenesis.² It primarily presents as vasculitis and arthritis secondary to systemic inflammation with immune-complex deposition.²

The diagnosis of SLE is typically made using the classification criteria set forth by the American College of Rheumatology and the European League Against Rheumatism, which use clinical symptoms and positive ANA titers.³ Thus, the diagnosis relies on the clinical presentation in the context of classification criteria, in combination with laboratory test findings suggestive of the disease.

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Classically, SLE is associated with musculoskeletal symptoms, cutaneous manifestations (rash and mucosal symptoms), nephropathies, and pulmonary/cardiovascular involvement,² but neuropsychiatric events are also common in the disease course, with an overall reported prevalence of 50%.⁴

Neurologic events can vary from mild lupus headache to severe manifestations such as lupus cerebritis. Yet of these neuropsychiatric manifestations, approximately only one-third can be medically attributable to SLE alone.⁵ Additionally, despite significant advances in recognition and treatment of SLE resulting in a global decline of mortality risk,¹ neuropsychiatric SLE (NPSLE) often presents a significant diagnostic and therapeutic challenge.⁵ An estimated 30% to 40% of persons with SLE will develop neuropsychiatric symptoms attributable to the disease, most often within the first 2 years of diagnosis.⁵ The most common manifestations include headache, mild cognitive impairment, and psychiatric/mood disorders. Seizures and ischemic cerebrovascular disease (including cardiovascular accidents and transient ischemic attacks) are also relatively common.⁵ Eye involvement is a known associated morbidity with SLE,⁶ but eye involvement secondary to cranial neuropathy and mononeuropathies are exceedingly rare, with an estimated cumulative occurrence rate of 0.5% to 1% and only a few reported cases in the literature.⁵ Treatment options for NPSLE vary based on the case presentation—high-dose glucocorticoids and further immunosuppression can be considered after other etiologies have been ruled out.

Isolated cranial nerve involvement is quite rare, such that this case of a patient previously diagnosed with SLE presenting with oculomotor nerve (cranial nerve III) palsy with only mild headache and fatigue is unique. It is important to note that differential diagnoses, including ischemia, neuromuscular dysfunction, and demyelination are all to be considered before attributing the pathology to SLE.

In one case series, 6 patients with oculomotor palsies (OMPs)—defined as those affecting the oculomotor nerve, the trochlear nerve (cranial nerve IV), or the abducens nerve (cranial nerve VI)—were studied in regards to laboratory data, immunologic test results, and cerebral imaging findings.⁷ Two of the patients had diffuse neurologic involvement, 2 patients had focal NPSLE manifestations involving multiple cranial nerves, and 2 had isolated abducens nerve palsies.⁷ This study is the largest case series involving OMPs in NPSLE, and the finding suggest that antiphospholipid antibodies (APLs) may mediate microthrombosis that could cause these OMPs. Other theories regarding the development of NPSLE include anti-*N*-methyl-D-aspartate (anti-NMDA) receptor antibodies,⁸ anti- β_2 glycoprotein I antibodies against cerebral endothelial cells,⁹ direct vascular injury of intracranial vessels leading to vasculitis,¹⁰ or autoantibodies with activity against neuronal cells.⁷

A case similar to our patient's was reported in which a 69-year-old woman with SLE in remission presented with isolated left

oculomotor nerve palsy.¹¹ Although SLE initially was the suspected etiology, 2 months after resolution of the patient's diplopia, she presented again with dysarthria and dysphagia, as well as left eye ptosis.¹¹ The diagnosis of myasthenia gravis was then made by positive acetylcholine receptor antibody test results and pathognomonic nerve-conduction study results.¹¹ However, during the episode of isolated oculomotor nerve palsy, the measured laboratory values—most notably serum complement levels—were within normal limits.¹¹ This finding differs from our patient's case of oculomotor nerve palsy in SLE, in which she demonstrated decreased serum complement levels.

The diagnosis of NPSLE is complicated by the variability of test results in these patients. Certainly, the onset of new neuropsychiatric symptoms in the context of previously diagnosed SLE should raise clinical suspicion.¹⁰ After exclusion of secondary causes, including infections or adverse drug reactions, further investigation is warranted with cerebrospinal fluid (CSF) analysis and neuroimaging via magnetic resonance imaging (MRI).¹⁰

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However, CSF abnormalities are nonspecific findings, while MRI scans revealing small subcortical or periventricular hyperintense T2-weighted focal lesions is not sensitive.¹⁰ Indeed, the results of neurologic workup with CSF analysis and MRI may be normal in 30% to 40% of patients with NPSLE,¹⁰ but the measured complement levels are often significantly decreased in the setting of an SLE flare such as in oculomotor nerve palsy.⁷ The diagnosis in our patient's case of isolated oculomotor nerve palsy was complicated by unremarkable CSF analysis findings and neuroimaging findings via MRI and CTA, but it was confirmed by low serum complement levels and improvement with corticosteroid therapy.

The goal of SLE therapy is clinical remission and prevention of flares at the lowest possible dose of corticosteroids.¹² The recommended treatment of SLE typically involves hydroxychloroquine, with regular ophthalmologic screening every 5 years

due to reported retinal toxicity.¹² Our patient had not been taking hydroxychloroquine because of concern about its potential adverse effect of retinopathy; it is unknown whether the lack of hydroxychloroquine therapy in this patient may have increased her risk of developing an SLE flare in the form of isolated oculomotor nerve palsy. Glucocorticoids are typically the first-line approach to resolving an SLE flare with minimal permanent damage; other treatment options can be added according to organ involvement and include methotrexate, azathioprine, mycophenolate, cyclophosphamide, biologic agents, dapsons, and cyclosporine.¹²

Biologic agents specifically targeting the neuronal immunologic activity responsible for NPSLE will likely be available in the future,⁶ but current treatment guidelines call for systemic

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immunosuppression via pulse corticosteroids followed by oral corticosteroid tapering, although significant atherothrombotic or antiphospholipid manifestations may require anticoagulation/antiplatelet therapy.¹² Furthermore, the 6 patients with OMPs in NPSLE in the published case series had significant improvement on corticosteroids alone, and the authors were unable to recommend long-term anticoagulation therapy for only these relatively minor focal neurologic symptoms without other characteristics of antiphospholipid syndrome such as venous thrombosis or spontaneous abortions.⁷ Our patient had initial improvement upon administration of high-dose pulse corticosteroids but not resolution of symptoms.

The recognition and treatment of neuropsychiatric manifestations in SLE requires clinical suspicion upon the development of central nervous system (CNS) symptoms in the context of existing SLE. After the exclusion of other etiologies, neurologic workup with CSF analysis, MRI, and serum antibody titers/complement levels can aid in the diagnosis of NPSLE. Previous studies suggest the treatment of NPSLE oculomotor nerve palsy with pulse corticosteroid therapy; indeed, our patient

improved upon the administration of high-dose pulse prednisone. This case emphasizes the importance of clinical recognition in NPSLE, even when faced with exceedingly rare CNS manifestations of the disease. ■

REFERENCES:

1. Stojan G, Petri M. Epidemiology of systemic lupus erythematosus: an update. *Curr Opin Rheumatol*. 2018;30(2):144-150. doi:10.1097/BOR.0000000000000480
2. Mok CC, Lau CS. Pathogenesis of systemic lupus erythematosus. *J Clin Pathol*. 2003;56(7):481-490. doi:10.1136/jcp.56.7.481
3. Gegenava M, Beart HJL, Monahan RC, et al. Performance of the proposed ACR-EULAR classification criteria for systemic lupus erythematosus (SLE) in a cohort of patients with SLE with neuropsychiatric symptoms. *RMD Open*. 2019;5(1):e000895. doi:10.1136/rmdopen-2019-000895
4. Bruns A, Meyer O. Neuropsychiatric manifestations of systemic lupus erythematosus. *Joint Bone Spine*. 2006;73(6):639-645. doi:10.1016/j.jbspin.2006.05.006
5. Bertias GK, Boumpas DT. Pathogenesis, diagnosis and management of neuropsychiatric SLE manifestations. *Nat Rev Rheumatol*. 2010;6(6):358-367. doi:10.1038/nrrheum.2010.62
6. Davies JB, Rao PK. Ocular manifestations of systemic lupus erythematosus. *Curr Opin Ophthalmol*. 2008;19(6):512-518. doi:10.1097/icu.0b013e3283126d34
7. Genevay S, Hayem G, Hamza S, Palazzo E, Meyer O, Kahn MF. Oculomotor palsy in six patients with systemic lupus erythematosus. A possible role of antiphospholipid syndrome. *Lupus*. 2002;11(5):313-316. doi:10.1191/0961203302lu205oa
8. Omdal R, Brokstad K, Waterloo K, Koldingsnes W, Jonsson R, Mellgren SI. Neuropsychiatric disturbances in SLE are associated with antibodies against NMDA receptors. *Eur J Neurol*. 2005;12(5):392-398. doi:10.1111/j.1468-1331.2004.00976.x
9. Meroni PL, Tincani A, Sepp N, et al. Endothelium and the brain in CNS lupus. *Lupus*. 2003;12(12):919-928. doi:10.1191/0961203303lu503oa
10. Bertias GK, Ioannidis JP, Aringer M, et al. EULAR recommendations for the management of systemic lupus erythematosus with neuropsychiatric manifestations: report of a task force of the EULAR standing committee for clinical affairs. *Ann Rheum Dis*. 2010;69(12):2074-2082. doi:10.1136/ard.2010.130476
11. Appenzeller S, Veilleux M, Clarke A. Third cranial nerve palsy or pseudo 3rd nerve palsy of myasthenia gravis? A challenging diagnosis in systemic lupus erythematosus. *Lupus*. 2009;18(9):836-840. doi:10.1177/0961203308101546
12. Fanouriakis A, Kostopoulou M, Alunno A, et al. 2019 update of the EULAR recommendations for the management of systemic lupus erythematosus. *Ann Rheum Dis*. 2019;78(6):736-745. doi:10.1136/annrheumdis-2019-215089