CASE REPORT

Monocular Oculomotor Nerve Disorder Manifesting as Cranial Neuropathy in Systemic Lupus Erythematosus

Kiyotaka Nakamagoe¹, Hisami Yanagia², Zenshi Miyake³, Yuya Kondo⁴, Takashi Hiyama⁵, Akiko Ishii¹, Yuichi Kaji⁶, Tetsuro Oshika⁶, Takayuki Sumida⁴ and Akira Tamaoka¹

Abstract:
We herein report the case of a patient who developed peripheral neuropathy of the bilateral lower legs that later became complicated with isolated oculomotor nerve disorder and was finally diagnosed as systemic lupus erythematosus (SLE). Based on the findings for oculomotor nerve paralysis and contrast-enhanced magnetic resonance imaging findings for the oculomotor nerve in the prepontine cistern, the isolated oculomotor nerve disorder was considered to be a manifestation of peripheral neuropathy. This oculomotor nerve disorder may contribute to the diagnosis of SLE and can be effectively treated with steroid pulse therapy. Reports of SLE manifesting as isolated oculomotor nerve paralysis are rare.

Key words: oculomotor nerve paralysis, pupillary dilatation, blepharoptosis, ophthalmalgia, systemic lupus erythematosus, cranial neuropathy

(Intern Med 57: 3445-3449, 2018)
(DOI: 10.2169/internalmedicine.1106-18)

Introduction

Systemic lupus erythematosus (SLE) is known to present as peripheral neuropathy, such as polyneuropathy, mononeuropathy, and cranial neuropathy. Cranial neuropathy is present in 7-12.7% of SLE patients with peripheral neuropathy (1, 2), and the diagnosis of unusual cranial neuropathy in some cases is difficult but important for obtaining an accurate SLE diagnosis. Isolated oculomotor nerve palsy is one type of cranial neuropathy seen with SLE (3). Peripheral neuropathy develops in 0.1% of patients during the period before SLE is diagnosed (1). In such cases, peripheral neuropathy, such as oculomotor nerve palsy, is difficult to diagnose and treat.

We herein report the case of a patient who developed peripheral neuropathy of the lower legs that later became complicated by isolated complete oculomotor nerve paralysis, which contributed to the final diagnosis of SLE as cranial neuropathy.

Beginning in 2015, a 61-year-old woman developed hypesthesia manifesting from the external side of the lower right leg to the right fourth and fifth toes. After several days, the muscular strength of the lower right leg decreased. After three months of walking with a cane and four months from the onset, the patient was hospitalized for the first time at our hospital. On hospitalization, the nearly symmetrical loss of sensation was evident in both legs, and muscle weakness and decreased tendon reflexes were apparent. She had a manual muscle testing score (out of a possible 5) of 5/5 for the iliopsoas, 5/5 for the quadriceps, 3/3 for the tibialis anterior, 3+/3 for the gastrocnemius, 2+/1 for the extensor hallucis longus, and 2+/1 for the flexor hallucis longus. The patient was unable to walk independently and used a wheelchair. In nerve conduction tests, the bilateral peroneal nerves, tibial nerves, and sural nerves were undetectable. The left sural nerve was biopsied. The densities of the large

¹Department of Neurology, Division of Clinical Medicine, Faculty of Medicine, University of Tsukuba, Japan, ²Department of Internal Medicine, Iwaki Kyoritsu Hospital, Japan, ³Department of Neurology, University of Tsukuba Hospital, Japan, ⁴Department of Rheumatology, Division of Clinical Medicine, Faculty of Medicine, University of Tsukuba, Japan, ⁵Department of Radiology, University of Tsukuba Hospital, Japan and ⁶Department of Ophthalmology, Division of Clinical Medicine, Faculty of Medicine, University of Tsukuba, Japan

Received: February 27, 2018; Accepted: April 8, 2018; Advance Publication by J-STAGE: July 6, 2018
Correspondence to Dr. Kiyotaka Nakamagoe, nakamagoek@md.tsukuba.ac.jp
and small myelinated fibers were severely decreased. Myelin ovoids were frequently observed. No small myelinated fiber cluster, onion bulb, or vasculitis was observed. The teased-fiber method revealed numerous myelin ovoids with findings suggestive of severe axonal damage. Based on the subacute progressive clinical course and findings of axonal peripheral neuropathy, and given the possibility of immune-mediated neuropathy such as acute motor sensory axonal neuropathy, two courses of immunoglobulin therapy were administered; however, the effects were limited, and the gait disturbance persisted.

Six months after the onset, right eye pain suddenly manifested. The next day, the patient was unable to open her right eye, and she was hospitalized again. At that time, right eyelid ptosis was noted. Her eye movement was characterized by impaired adduction and upward and downward rotation. Her corrected visual acuity was normal. The right pupil was also dilated, and both the direct and indirect light reflexes had disappeared (Fig. 1A). These findings resulted in a diagnosis of right-eye oculomotor paralysis. Magnetic resonance imaging (MRI) of the head showed a contrast effect at the right oculomotor nerve in the prepontine cistern (Fig. 1C).

The present case met a number of Systemic Lupus International Collaborating Clinics criteria (4). These included neurological abnormalities in the form of peripheral and cranial nerve disorders as well as leukopenia and lymphopenia. Immunological tests also showed positive results for antinuclear antibodies, double-stranded DNA antibodies, hypocomplementemia, and a direct Coombs test. Systemic lupus erythematosus was diagnosed based on those findings. The patient had no organ damage except for peripheral neuropathy and nephropathy; a urinalysis showed albuminuria (135.2; normal range <30 mg/g·Cre), elevated N-acetyl-β-D-glucosaminidase (NAG) (25.9; normal range <15.0 U/g·Cre), and elevated β-2 microglobulin (567; normal range <230 μg/L).

Based on the diagnosis of SLE, 3 courses of steroid pulse therapy (methylprednisolone 1,000 mg/day for 3 days) were administered at 1-week intervals. Eye pain was the first symptom to disappear after starting this treatment; this was followed by improvements in the pupil dilation, light reflexes, and ptosis. The oculomotor nerve palsy also gradually improved, in the order of ocular upward/downward rotation and then adduction. Two weeks after completion of the third course of pulse therapy, the patient’s ptosis and pupil abnormality had nearly recovered; however, her eye movement was still impaired. Following the completion of pulse therapy, oral prednisolone was continued at 30 mg/day. MRI performed three months after starting steroid therapy showed attenuation of the earlier contrast effect at the right oculomotor nerve (Fig. 1D). Nine months after starting steroid therapy, the right oculomotor nerve palsy had completely resolved (Fig. 1B).
most common in oculomotor nerve palsies (8, 9). Ocular pain might be induced by inflammation of a blood vessel around the oculomotor nerve.

Alternatively, antiphospholipid syndrome may be associated with an isolated pupil-sparing oculomotor nerve palsy due to midbrain infarction (10).

Based on the findings from the previous report (3) and the present case, the characteristics of an isolated oculomotor nerve disorder as cranial neuropathy in SLE patients might be accompanied by a contrast-enhanced oculomotor nerve on MRI and clinical findings such as blepharoptosis and pupillary abnormalities (Fig. 2). Furthermore, this characteristic oculomotor nerve disorder may contribute to the diagnosis of SLE as cranial neuropathy.

The authors state that they have no Conflict of Interest (COI).
Oculomotor nerve disorder manifesting as cranial neuropathy in systemic lupus erythematosus

Financial Support
This work was supported by JSPS KAKENHI Grant Number JP 26460901.

References
1. Lee JS, Roh YB, Oum BS, et al. Isolated oculomotor nerve palsy with pupillary abnormality in systemic lupus erythematosus. J Pediatr Ophthalmol Strabismus 37: 241-243, 2000.
2. Xianbin W, Mingyu W, Dong X, et al. Peripheral neuropathies due to systemic lupus erythematosus in China. Medicine (Baltimore) 94: e625, 2015.
3. Toledano P, Orueta R, Rodríguez-Pintó I, et al. Peripheral nervous system involvement in systemic lupus erythematosus: prevalence, clinical and immunological characteristics, treatment and outcome of a large cohort from a single centre. Autoimmun Rev 16: 750-755, 2017.
4. Petri M, Orbai AM, Alarcón GS, et al. Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. Arthritis Rheum 64: 2677-2686, 2012.
5. Blake PY, Mark AS, Kattah J, et al. MR of oculomotor nerve palsy. AJNR Am J Neuroradiol 16: 1665-1672, 1995.
6. Capó H, Warren F, Kupersmith MJ. Evolution of oculomotor nerve palsies. J Clin Neuroophthalmol 12: 21-25, 1992.
7. Sanders S, Kawasaki A, Purvin VA. Patterns of extraocular muscle weakness in vasculopathic pupil-sparing, incomplete third nerve palsy. J Neuroophthalmol 21: 256-259, 2001.
8. Galtrey CM, Schon F, Nitkunan A. Microvascular non-arteritic oculomotor nerve palsies-what we know and how should we treat? Neuroophthalmology 39: 1-11, 2014.
9. Wilker SC, Rucker JC, Newman NJ, et al. Pain in ischaemic oculomotor cranial nerve palsies. Br J Ophthalmol 93: 1657-1659, 2009.
10. Champion BL, Choy F, Schrieber L, et al. Isolated fascicular ocu-
Lumbar nerve palsy as the initial presentation of the antiphospholipid syndrome. J Clin Neurosci 9: 691-694, 2002.