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Case Report

Acute Foot Drop in the Initial Presentation of Systemic Lupus Erythematosus

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Abstract

The case of a 20-year-old woman with newly diagnosed systemic lupus erythematosus (SLE) who developed acute foot drop secondary to mononeuritis multiplex is presented. Peripheral neuropathy etiology is broad, but in the setting of SLE, it should raise concern for vasculitis, as seen in this case with mononeuritis multiplex. Diagnosis requires an understanding of SLE pathology as seen with muscle and nerve biopsy. Prompt diagnosis and high-dose corticosteroids are critical, but pain may persist despite immunosuppression.

Keywords: Foot drop, mononeuritis multiplex, neuropathic pain, peripheral neuropathy, systemic lupus erythematosus (SLE), vasculitis

Introduction

Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease characterized by autoantibody production and immune complex deposition leading to inflammation and damage, classically to the skin, joints, kidneys, hematologic system, and central nervous system (CNS).[1,2] However, SLE has also been associated with peripheral nervous system involvement, causing peripheral neuropathy presenting as motor, sensory, or mixed fiber polyneuropathy, isolated mononeuropathy, or mononeuritis multiplex.[3,4,5]

One presentation of peripheral neuropathy is foot drop or weakness in ankle dorsiflexion. The differential diagnosis for foot drop is broad and includes central causes such as stroke, multiple sclerosis, and spinal cord lesions/compression; radiculopathies involving L5; and peripheral nerve injuries, most commonly compression of the common peroneal nerve at the fibular head, but also including lumbosacral plexopathy. Additionally, systemic conditions such as diabetes mellitus or vasculitis are also part of the vast differential. Less commonly, there are hereditary neuropathies such as Charcot–Marie–Tooth, neuromuscular junction disorders, and distal myopathies, which may present with isolated foot drop.[6]

Here, a case of foot drop in a patient with newly diagnosed SLE who underwent an extensive workup to reveal mononeuritis multiplex in the setting of SLE is presented.

Case Presentation

Informed consent was obtained from the patient for case report publication.

A 20-year-old woman was admitted for symptoms of left lower foot numbness/pain and weakness, which had been ongoing for 2 months prior to admission (Figure 1). Over the last 3 months before admission, she experienced polyarthralgia, worse in her knees, along with various scattered papules on the left elbow, intermittent low-grade fevers to 100.4. She was evaluated by Rheumatology 1 month prior to admission, with initial testing showing positive DS-DNA, ANA, SSA, and Smith autoantibodies. She was started on prednisone 10 mg and hydroxychloroquine 400 mg daily. A subsequent rheumatology visit revealed worsening joint pain, calf cramping in her left leg worse than the right, and a new inability to dorsiflex her left foot, prompting transfer to the emergency department (ED). In the ED, she was found to be in significant pain. On examination, she was noted to have swelling of her feet bilaterally; tenderness to light touch; 0/5 dorsiflexion, plantar flexion, and inversion of the left foot.

On arrival, spinal pathology was evaluated with magnetic resonance imaging of the lumbar spine, which showed: mild degenerative disc disease primarily localized to the L3-L4 and L4-L5 levels, along with mild spinal canal stenosis at L3-L4 and L4-L5. Importantly, no focal nerve root impingement or foraminal stenosis

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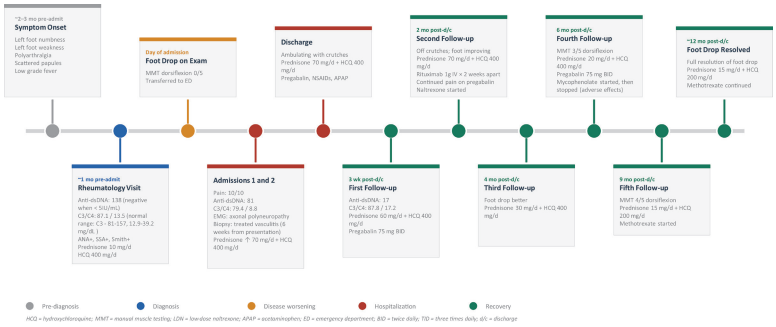

Figure 1. Clinical timeline. Acute foot drop as initial presentation of systemic lupus erythematosus due to mononeuritis multiplex.

was identified. Magnetic resonance imaging of her left leg showed preserved peripheral nerve anatomy without compressive lesions, along with multiple chronic or indeterminate musculoskeletal findings and diffuse muscular edema. She was discharged home.

Following 2 weeks of worsening pain, the patient was readmitted for further studies. Electrodiagnostic studies revealed a severe length-dependent, axonal, sensorimotor polyneuropathy with absent sensory responses in the left sural and superficial peroneal nerves and absent or markedly reduced motor responses in the peroneal and tibial nerves. Findings in peroneal-innervated muscles raised concern for superimposed tibial and peroneal mononeuropathies versus sciatic neuropathy, though technical limitations may have affected interpretation.

During this second admission, approximately 6 weeks from her initial outpatient presentation, neurosurgery was performed on the left sural nerve and gastrocnemius muscle biopsy. Pathology of the sural nerve revealed moderately dense perivascular lymphocytic inflammatory infiltrate involving small and medium caliber blood vessels with significant nerve fiber damage, including loss of myelinated axons and myelin ovoids (Figure 2). This raised concern for an underlying vasculitis. Gastrocnemius muscle biopsy showed type 2 atrophy.

Rheumatology advised increasing the prednisone dose to 70 mg daily and continuing hydroxychloroquine 400 mg daily. Over the 10-day hospital course, weakness minimally improved. Pain control proved difficult, and she was seen by the acute pain service for a ketamine infusion. Following discharge, the patient was followed by rheumatology and pain medicine. In the outpatient setting, the prednisone dose was slowly tapered. She was given 2 doses of rituximab. Her weakness continued to improve, and she was no longer using crutches 2 months following hospitalization. By the 4-month mark, the patient was walking without devices and on exam was noted to have 3/5 strength. Pain medicine started the patient on low-dose naltrexone (LDN) along with pregabalin around 2 months post discharge. Over the next few months, she had significant pain relief on LDN with pain rated at 0/10 during the office visit 5 months after discharge. At the 6-month follow-up, as corticosteroids were tapered, mycophenolate mofetil was initiated but subsequently discontinued due to adverse effects. At the 9-month follow-up, methotrexate was started for improved control of SLE. By the 10-month mark, the patient's foot drop and pain had fully resolved.

Discussion

Peripheral neuropathy due to SLE is less common compared to classic CNS presentations.[7] As a result of the large differential of peripheral neuropathy, diagnosis can be challenging, especially in the early onset of SLE. In this case, the patient lacked any peripheral injury or central etiologies, which allowed a focused approach related to SLE.

Mononeuritis multiplex is an immune-mediated vasculitis targeting the vasa nervorum, causing asymmetric damage to 2 or more peripheral nerves. The inflammation and destruction of the blood vessels supplying these peripheral nerves leads to ischemic injury.[8] Histopathologically, nerve biopsy often will reveal perivascular lymphocytic infiltrates, fibrinoid necrosis of vessel walls, and evidence of ischemic axonal damage.[8] In the biopsy obtained during the patient's hospitalization, there was a perivascular lymphocytic infiltrate of the vessels with significant nerve fiber damage. However, the biopsy was taken roughly 1 month after starting prednisone, which is the suspected reason why fibrinoid necrosis was absent.

Management of mononeuritis multiplex in SLE is centered on prompt immunosuppression, with high-dose corticosteroids being first-line therapy.[9] Guidelines from the American College of Rheumatology and the European League Against Rheumatism support the use of corticosteroids with or without further immunosuppression for SLE vasculitis.[10] Prior case reports make use of cyclophosphamide, which was deferred, given the patient is of reproductive age.[11] Two doses of rituximab 1 g were given, separated by 2 weeks, with significant improvement in symptom control and pain. While rituximab is often used for SLE with extrarenal manifestations, there are few formal studies looking at mononeuritis multiplex. Rituximab, a chimeric monoclonal antibody, binds to CD20 antigen on B cells, leading to their elimination through mechanisms such as complement-dependent cytotoxicity, antibody-dependent cell-mediated cytotoxicity, and induction of apoptosis. This B cell depletion reduces the production of pathogenic autoantibodies and immune complexes, which are key drivers of vascular inflammation and nerve injury in SLE-associated mononeuritis multiplex.[12] In published case series, patients

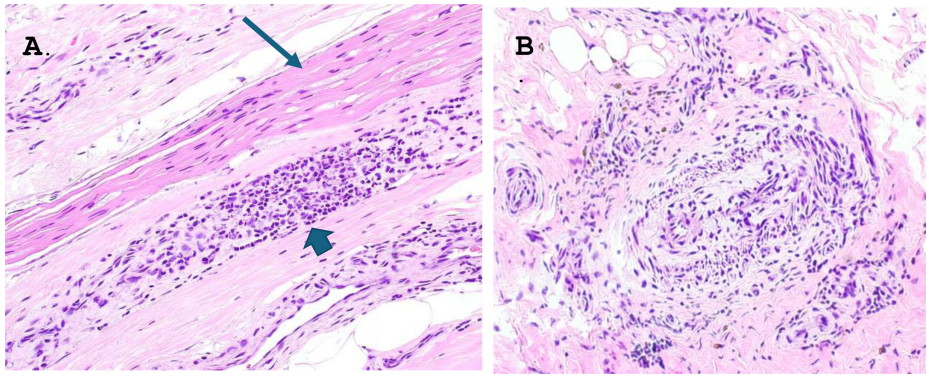

Figure 2. (A) Longitudinal section of nerve (thin arrow) with chronic lymphocytic infiltrates in the epineural compartment (thick arrow; 20×). (B) Cross-section of an abnormally small-to-medium-sized blood vessel with myxoid and fibrotic histologic features consistent with a treated vasculitis (40×).

with SLE-associated mononeuritis multiplex who have been treated with rituximab, along with steroids and other immunosuppressants, have shown clinical improvement.[13] However, the number of reported cases is small, with this case adding to the body of literature.

The initial discharge pain plan for the patient made use of gabapentinoids, non-steroidal anti-inflammatory drugs (ibuprofen, naproxen) and opioids. However, pain control proved difficult. Given the exhaustion of classic therapies, the patient was started on LDN, which provided significant pain relief. Low-dose naltrexone provides antagonism of toll-like receptor 4 on microglial cells, leading to reduced neuroinflammation and decreased cytokine release. Of note, this is different from naltrexone's classic role as a mu-opioid.[14]

The case has several limitations worth acknowledging. As a single case report, generalizability is limited. The sural nerve biopsy was obtained approximately 1 month after corticosteroids were initiated, which may contribute to the absence of fibrinoid necrosis and underrepresent the true degree of vascular inflammation at disease onset. Further case series and prospective studies are needed to better characterize optimal management of this rare complication.

Overall, this case highlights the broad impact of SLE and its presentation of peripheral neuropathy, along with the diagnostic approach to confirm mononeuritis multiplex.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

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