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Case Study

Extensive Longitudinal Transverse Myelitis in Systemic Lupus Erythematosus: Case Report and Review of Current Literature

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Received: November 05, 2024; **Published:** November 20, 2024

Abstract

Acute transverse myelitis (TM) is an inflammatory condition that presents with quickly advancing motor, sensory, and autonomic symptoms, which can have severe consequences. The three leading causes of acute TM are demyelinating diseases, infections, and autoimmune inflammatory conditions like systemic lupus erythematosus (SLE). The American College of Rheumatology (ACR) includes TM as one of the 19 neuropsychiatric conditions linked with SLE, with an incidence rate of about 1 - 2% among SLE cases. Misdiagnosis is common, often resulting in high morbidity and mortality. This report examines the case of a 23-year-old woman with progressive muscle weakness in her lower limbs, dysesthesias from the abdomen to the feet, and loss of sphincter control. On examination, severe paraparesis with sensory level at T8 was identified. MRI of the thoracolumbar spine showed hyperintensity on T2 and STIR sequences from T7 to L1, consistent with TM. Due to resistance to initial treatment, cyclophosphamide was administered. After a week in the hospital, the patient showed partial neurological improvement. Recognizing TM in SLE patients requires high clinical suspicion, and early intervention is crucial to minimize severe complications and reduce the rates of morbidity and mortality.

Keywords: *Transverse Myelitis; Neuropsychiatric Lupus; Cyclophosphamide; Autoimmune*

Introduction

Acute Transverse Myelitis (TM) is a rapidly progressing inflammatory disease affecting motor, sensory, and autonomic functions, often leading to serious outcomes. The primary causes of acute TM include demyelinating diseases, infections, and autoimmune inflammatory disorders, such as systemic lupus erythematosus (SLE). Neurological and psychiatric symptoms associated with SLE (NPSLE) are diverse and are often linked with poor prognosis. Studies based on the American College of Rheumatology's (ACR) classification report a prevalence rate of 37% to 95% for NPSLE [1]. This wide range may be due to factors such as the inclusion of minor symptoms, lack of a standard for diagnosis, and the challenges of attributing events to either primary NPSLE or secondary causes (like infections, medications, metabolic changes, and multiorgan damage). TM, one of the 19 NPSLE syndromes classified by ACR in 1999, appears in 1 - 2% of SLE cases [2]. TM in SLE cases is often severe; one-third of patients experience symptoms as an early indicator, though it can occur up to three years after diagnosis. Recurrence of TM ranges from 18% to 50%. In Colombia, the prevalence of SLE is about 9.19 per 10,000 people, comparable to other Latin American countries [3]. Myelitis affects between 1% and 2% of SLE patients and is about 1,000 times more common than idiopathic myelitis in the general population [2]. SLE-associated TM can involve grey matter, leading to hypotonia and hyporeflexia, or white matter, resulting in irreversible myelitis with spasticity and hyperreflexia. SLE-related TM has high morbidity, and rapid treatment with corticosteroids and cyclophosphamide can improve outcomes. However, due to limited awareness of its clinical presentations, SLE-

related TM is often underdiagnosed [4]. This case report details a severe, longitudinal episode of TM in SLE, where early clinical suspicion, timely imaging, and prompt therapeutic intervention enabled a full recovery.

Case Presentation

A 23-year-old woman with no significant medical history, aside from autoimmune hemolytic anemia requiring transfusion and treatment with prednisolone, arrived at our hospital's emergency department. She reported experiencing lower back pain, polyarthralgia, and progressive muscle weakness in her lower limbs. Over the past two weeks, she had also noticed a loss of bladder and bowel control and dysesthesias extending from her abdomen down to her feet. On examination, her temperature was normal at 37°C, and her blood pressure was 135/80 mmHg. Respiratory, cardiac, abdominal, and joint exams were unremarkable. Neurological assessment revealed a muscle strength of 1/5 in the lower limbs and 5/5 in the upper limbs, with reduced sensitivity to pain, touch, and temperature at the T8 dermatome level. Cranial nerve examination showed no abnormalities, but she had red, raised, scaly plaques on her skin. A lumbar puncture revealed clear fluid without pleocytosis, a glucose level of 53 mg/dL (normal range: 40 - 80 mg/dL), with a concurrent blood glucose level of 112 mg/dL, and total protein at 83 mg/dL (normal range: 40 - 60 mg/dL). Cerebrospinal fluid (CSF) tests for infections were negative. Her ANA antibodies were positive, anti-DNA antibodies were measured at 1664 IU/mL, with C3 at 36 mg/dL and C4 at 6.6 mg/dL.

With a suspicion of complete spinal cord syndrome, an MRI was performed, which ruled out extramedullary compression and showed a mild increase in spinal cord diameter, along with T2 and STIR hyperintensity from T7 to L1. These findings were consistent with a longitudinally extensive TM (Figure 1). Treatment was initiated with high-dose methylprednisolone at 1 gram per day for two days.

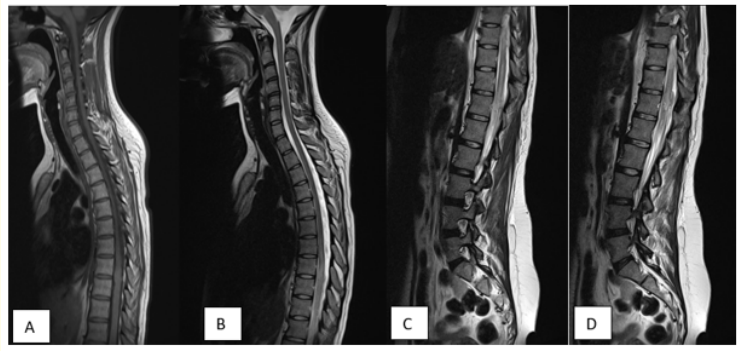

Figure 1: *Sagittal T1 slices (A) and sagittal T2 slices (B, C, D) of a spinal MRI showing an increase in spinal cord diameter with a T2 hyperintensity extending from T7 to L1.*

Discussion

Systemic lupus erythematosus (SLE) is a complex multisystem disorder with the potential to impact any organ. Its most common manifestations involve the skin and joints, though renal involvement and neuropsychiatric manifestations (NPSLE) are also significant. The presence of NPSLE often correlates with more severe disease and affects the overall prognosis [5]. NPSLE encompasses a range of neurological and psychiatric complications attributed to SLE, posing diagnostic challenges due to its broad spectrum and variability in clinical presentation [6]. In 1999, the American College of Rheumatology (ACR) categorized NPSLE into 19 distinct syndromes, dividing them into central nervous system (CNS) manifestations-further classified into focal and diffuse-and peripheral nervous system (PNS) manifestations. Among the focal CNS manifestations is transverse myelitis (TM), which represents more than just a pathological or

radiological spinal lesion. TM reflects acute or subacute spinal cord dysfunction on a sensory level and, if complete, results in motor and autonomic impairments (affecting bladder, bowel, and sexual function) below the lesion level. Partial TM, on the other hand, involves either motor or sensory deficits but not both [7].

The pathogenesis of NPSLE remains incompletely understood, but small-vessel vasculitis and thrombosis, as suggested by pathological and serological findings, likely contribute to axonal injury through ischemia and necrosis. In cases of TM, the spinal level and extent of involvement may indicate which pathophysiological mechanisms are at play. Thoracic involvement is common, given that this segment contains smaller caliber vessels in the spinal vasculature and is thus more vulnerable to thrombosis. If antiphospholipid antibodies (aPL) are present, this might suggest a thrombotic mechanism at work [8]. Studies show that among NPSLE patients with TM, between 50% and 100% have associated aPL antibodies. For example, Katsiari CG., *et al*. (2011) reported no benefit from anticoagulant therapy in such cases [9]. This association underscores the importance of testing for these antibodies, as they may heighten the risk of neurological complications in SLE patients. Additionally, some SLE patients are seropositive for anti-aquaporin 4 (AQP4) antibodies, which are specific markers for neuromyelitis optica (NMO). These antibodies induce direct CNS injury through astrocytic damage via complement- and antibody-dependent cytotoxicity. The presence of AQP4 during an initial TM episode suggests a higher likelihood of recurrence and possible optic neuritis development within the year. While AQP4 positivity in SLE is relatively low (2-3%), it is significantly higher (27%) in NPSLE cases [10]. The International Consensus on NMO Spectrum Disorders suggests that, in cases where AQP4 testing is unavailable, diagnosis can rely on clinical evaluation, two core clinical criteria, and ruling out alternative diagnoses [11]. In the case described, there was no evidence of NMO-associated regional CNS spread or symptomatic cerebral or area postrema involvement at the onset of myelitis. There was also no further CNS involvement in the six clinical regions of interest for NMO diagnosis prior to the patient's passing.

Regarding diagnosis, the ACR defined lupus-associated TM diagnostic criteria in 1999. Based on the clinical picture, affected patients present with acute or subacute paraplegia or quadriplegia, typically bilateral but not always symmetrical, along with a sensory level identified at the spinal level, and/or bowel or bladder dysfunction. Rapid neuroimaging is essential to rule out spinal cord compression. Contrast-enhanced MRI is the diagnostic tool of choice for confirming TM and ruling out other causes, such as spinal cord hemorrhages or tumors. Longitudinal spinal involvement (71%) is more common than transverse involvement (28%) in imaging studies [4]. CSF findings may include lymphocytic pleocytosis and slightly reduced glucose levels (usually > 30 mg/dL). However, normal CSF results do not exclude TM.

Two TM subtypes are reported based on clinical and imaging findings: gray matter TM, which presents with fever, flaccid weakness, hyporeflexia, and urinary retention, with rapid onset. This subtype is linked to anti-DNA antibodies. White matter TM is associated with positive aPL antibodies, recurrent thrombosis, and anti-Ro/SSA antibodies. In Birnbaum J., *et al*.'s 2009 cohort, overlap between TM-SLE and NMO showed predominant white matter involvement, with a history of optic neuritis, longitudinal TM (>3 vertebral segments), recurrent relapses, and MRI findings not characteristic of multiple sclerosis. White matter TM is often recurrent, while gray matter involvement tends to show a monophasic recurrence pattern. In a subset of antiphospholipid syndrome (APS) patients, white matter lesions with positive lupus anticoagulant are found in over half, whereas gray matter involvement is under 20%. Anti-DNA and anti-Ro/SSA antibodies did not significantly differ between these groups [12]. The case described did not meet NMO or APS criteria, and, although mixed features were present, gray matter involvement was predominant.

As for treatment, the European League Against Rheumatism (EULAR) recommends initiating IV methylprednisolone and cyclophosphamide early for NPSLE, ideally within hours of symptom onset, even if CSF findings suggest possible meningitis while awaiting microbiological results. This combination is considered the standard treatment for this neuropsychiatric complication. Typical doses include IV methylprednisolone pulses of 1 gram daily for three days, combined with IV cyclophosphamide at 0.75 - 1 g/m^2 monthly for six months, followed by every three months for a year, alongside oral prednisone at 1 mg/kg/day starting on day four, tapering over

1-3 months. Plasmapheresis may be added for refractory cases, although it does not appear to improve prognosis [13]. IV immunoglobulin has also been employed in initial or refractory cases, either alone or with standard therapy. Anticoagulation, while used in aPL-positive TM cases, has not shown additional therapeutic benefit beyond immunosuppression. Emerging data on biologics like rituximab, alone or combined with cyclophosphamide, show promise but require larger studies [14].

Maintenance therapy options include azathioprine, methotrexate, or mycophenolate combined with low-dose steroids, generally recommended for three years or longer; however, the optimal duration is not yet defined.

Conclusion

SLE can sometimes cause a serious neurological consequence called longitudinal extensive transverse myelitis (MTLM). The literature is significantly lacking in information on clinical course, outcomes and therapeutic efficacy. Infections, demyelinating conditions, and compressive tumors are all included in the broad differential diagnosis of MTLET. Due to the clinical and prognostic importance of MT-SLE, immediate recognition and intervention is needed to prevent catastrophic outcomes that occur in up to one-third of patients. If clinical improvement is not achieved with initial corticosteroid therapy, the addition of immunomodulatory management including cyclophosphamide or plasmapheresis should not be delayed because of its favorable impact on disability and survival, especially in refractory cases. Our patient had a TML and had substantial neurological deterioration. Timely intervention resulted in a remarkable gradual recovery of function, and our SLE patient was able to walk and recover sphincter function and sensation without long-term sequelae.

Conflicts of Interest

The authors declare no conflicts of interest.

Author Contributions

Dr. Ajertil is the primary author, and Professor El Quessar contributed to the development of this work by providing her expertise in writing.

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Volume 16 Issue 12 December 2024

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