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Case Report

Longitudinal Myelitis Associated With Systemic Lupus Erythematosus☆

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ABSTRACT

A case is presented of a 33 year-old woman diagnosed with longitudinal myelitis secondary to systemic lupus erythematosus. She presented with paraplegia and hypoesthesia to pain, and temperature sensitivity to dermatome level T6. She was treated with pulses of methylprednisolone and cyclophosphamide, with partial response to treatment. Myelitis is an inflammatory disease that causes injury to the spinal cord. Longitudinal myelitis refers to the continued involvement of the spinal cord, with the involvement of three or more adjacent spinal segments. The treatment consists of high steroid doses, sometimes combined with immunosuppressants and/or plasmapheresis.

Mielitis longitudinal asociada a lupus eritematoso sistémico

Palabras clave:
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Mielitis longitudinal
Lupus eritematoso sistémico

RESUMEN

Se presenta el caso de una mujer de 33 años de edad con el diagnóstico de mielitis longitudinal secundaria a lupus eritematoso sistémico. Presentó paraplejía e hipoestesia para sensibilidad térmica y dolorosa a nivel del dermatoma T6, recibió manejo con pulsos de metilprednisolona y ciclofosfamida con respuesta parcial al tratamiento. La mielitis es una enfermedad inflamatoria que produce una lesión en la médula espinal, la mielitis longitudinal hace referencia a la participación continua de la médula espinal, con implicación de 3 o más segmentos medulares contiguos. El tratamiento consiste en dosis altas de glucocorticoides combinados o no con inmunosupresores o plasmaféresis.

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Introduction

In 1999, the American College of Rheumatology published 19 neurological syndromes associated with systemic lupus erythematosus (SLE), dividing them into 2 categories: central and peripheral.[1] Myelopathy is a manifestation of central type, which affects less than 1% of patients with SLE.[2,3] It is very serious and usually can appear within the first 5 years of evolution of the disease, with a recurrence of 21-55%, and 21% of patients do not improve and even show deterioration once treatment is established.[4,5] The management consists in the combination of methylprednisolone and cyclophosphamide intravenously, being more effective the sooner it is started; the plasma exchange therapy is used in cases that are severe or refractory to the initial treatment.[6]

Clinical Case

A 33 years old female patient diagnosed with SLE one year ago (non-erosive polyarthritis, malar erythema, pancytopenia, mucosal affectation and positive antinuclear and anti-DNA antibodies) under treatment with glucocorticoid, azathioprine and hydroxychloroquine. The patient is admitted because of loss of alertness, as well as fever of 72 hours of evolution and headache with occipital predominance, 2 days early she had diarrheic stools, nausea and vomiting. Physical examination reveals malar erythema, disorientation, presence of meningeal signs (nuchal rigidity, positive Kernig's and Brudzinski's signs). The paraclinical tests on admission report normocytic, normochromic anemia (Hb 10 g/dL, Hct 35.8%, MCV 87.8 fL, MCH 27.1 pg), leukocytes 10.2 × 10^3/µ, blood biochemistry, serum electrolytes and clotting times within normal parameters.

Meningitis is suspected because of the clinical picture, and is performed a lumbar puncture which reports hyperproteinorrachia (198 mg/dL), hypoglycorrhachia (24 mg/dL), cell count 1,500 cells/mm^3, 74% polymorphonuclear cells, Gram and AFB stains negative. With the diagnosis of bacterial meningitis, an empirical treatment with ceftriaxione 2 g, every 12 hours is started, pending the result of the cerebrospinal fluid (CSF) culture.

After 24 hours of treatment, the patient presents recovery of alertness, absence of headache and meningeal signs. 48 hours after starting treatment she has paresthesias and ascending weakness in lower limbs, as well as urinary and bowel retention, and hypotonic anal sphincter. At 72 hours she has paraplegia, lower limb muscle strength 0/5 in Daniels' scale, level hypoesthesia for thermal and pain sensitivity initially in dermatome L1, ascending to T6 within 24 hours.

Upon clinical suspicion of a myelitis associated with SLE, a nuclear magnetic resonance (MRI) of the spinal cord is performed urgently, which reports spinal cord widening in T1 sequence (Fig. 1), and spinal cord widening with hyperintense signal in the entire length of the thoracic and lumbar spine in the T2 sequence (Fig. 2), with the confirmation of a longitudinal myelitis, pulses with 1 g of methylprednisolone intravenously, every 24 hours, 3 doses, are started, followed by 1 g of cyclophosphamide intravenously, after previous administration of Mesna. Since transverse myelitis is a typical finding in neuromyelitis optica, anti-aquaporin 4 (anti-AQP4) IgG antibodies in serum are requested, with negative results.

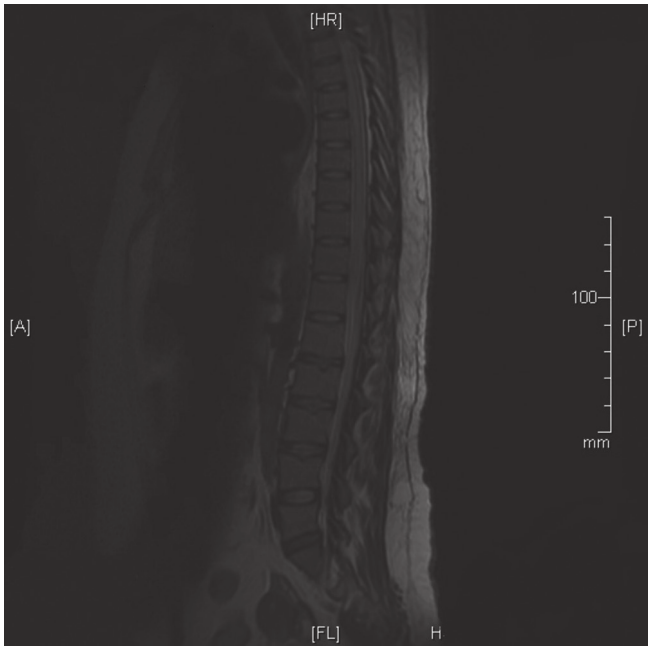

Figure 1 – Magnetic resonance imaging of the thoracic and lumbar spinal cord in T1 sequence, where we can observe the spinal cord widening in its entire length.

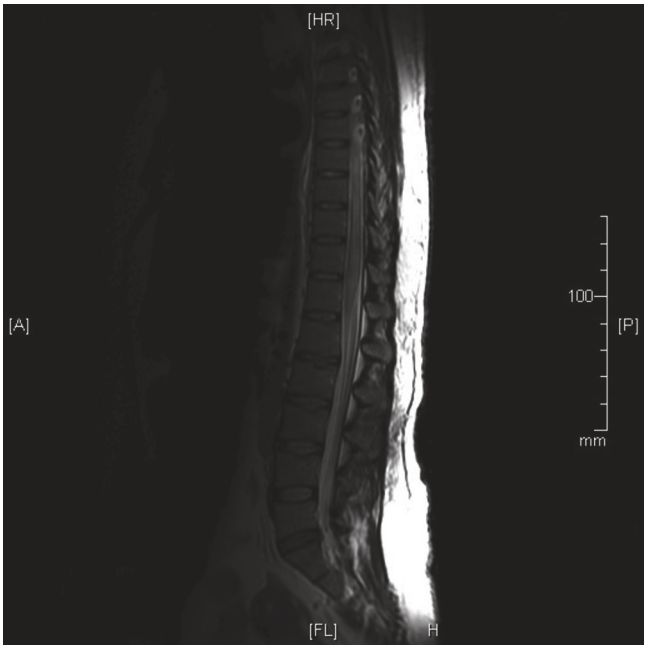

Figura 2 – Magnetic resonance imaging of the thoracic and lumbar spinal cord in T2 sequence, in which spinal cord widening and hyperintense signal can be observed in its entire length.

The result of CSF culture for bacteria, fungi and *Mycobacterium tuberculosis* is collected with negative results.

Antiphospholipid antibodies (aPL) are requested, which report anti-cardiolipin (aCL) IgG antibodies of 40 U/mL, aCL IgM 25 U/mL, anti-β2 glycoprotein (β2GPI) IgG antibodies of 90 U/mL, IgM anti-β2GPI 115 U/mL. Low-dose aspirin is added to management.

After the pulses, she is maintained on prednisone at doses of 75 mg/day, orally, and 50 mg of azathioprine.

Seven days after the beginning of the pulses, the patient recovers the sensitivity at the level of L1, but continues with paraplegia and incontinence of sphincters. After 6 cycles of cyclophosphamide, one monthly, the patient regains the control of sphincters, but remains with paraplegia; without relapse after 7 months of follow-up.

Discussion

We present the case of a 33 year old woman with longitudinal myelitis secondary to SLE, initially it was thought that it was a bacterial meningitis due to the presence of meningeal signs and the characteristics of the CSF, however, when paraplegia appeared, a MRI scan of the spinal cord was performed, confirming the diagnosis of longitudinal myelitis.

The term longitudinal myelitis is used when there is continuous involvement of the spinal cord or when 3 or more adjacent segments of the spinal cord are involved, it centrally affects the spinal cord, and sometimes, it extents to the medulla oblongata, being observed with better definition on T2 and STIR sequences of MRI. If the spinal cord involvement appears hypointense on T1, it indicates necrosis and cavitation (sequelar injury), while if it shows reinforcement with gadolinium it indicates active inflammation.[7,8]

Neuropsychiatric lupus (NPSLE) occurs in up to 80% of patients, however, myelitis is infrequent and occurs in 1%. Until the year 2009, 105 cases of myelitis associated to SLE had been reported in literature.[3]

NPSLE is one of the leading causes of morbidity and mortality in patients with SLE; it is multifactorial, involving inflammatory cytokines, autoantibodies and immune complexes. In the autopsies of patients with NPSLE, multifocal infarcts, cerebral hemorrhage, cortical atrophy, demyelination and ischemia are observed. The integrity of the blood-brain barrier and the presence of autoantibodies play an important role in the physiopathogenesis.[9]

Many autoantibodies have been described in the serum of patients with SLE, however, in NPSLE, only 3 have been associated with clinical manifestations: aPL, anti-ribosomal P protein, and the anti-NR2 subunit of the glutamate N-methyl-D-aspartate receptor antibodies.[9] The aPL are present in up to 60% of patients with myelitis associated with SLE.[3,8] Due to the presence of these antibodies is thought that the pathophysiological mechanism is the consequence of arterial thrombosis, which produces necrosis of the spinal cord, as well as a direct interaction between the antibodies and the spinal phospholipids.[10]

Its clinical presentation can be as an acute or subacute myelitis, when it evolves within more than 4 hours and less than 4 weeks, or it can be a progressive chronic myelitis with a syndrome of remissions and relapses of spinal cord involvement.[4,6] In the acute and subacute forms, the patient experiences intense pain at the level of the neck and in the interscapular region, subsequently appear sensory and motor deficits below the level of the spinal cord lesion; the subacute and chronic forms use to be more associated with urinary incontinence and gait difficulty, which can progress to spastic paraplegia. The myelitis associated with SLE usually occurs with paraplegia in up to 70% of cases, swelling of the affected area, urinary retention and abdominal or low back pain.[6,8]

Diagnosis can be made by imaging studies of the spinal cord and CFS studies. The MRI shows hyperintense signals in 70-93% of cases; gadolinium enhancement and edema of the spinal cord, as well, are useful to exclude cord compression.[6] If other signs or symptoms of NPSLE appear, a brain MRI scan should be performed. Mild to moderate CSF abnormalities are common (50-70%), but not specific, there are usually pleocytosis, hypoglycorrhachia and hyperproteinorrachia; microbiological studies should be performed to exclude infectious myelitis.[3,6]

The differential diagnosis should be made with viral infections, spinal cord compression due to vertebral fractures, epidural or subdural lipomatosis, paravertebral abscesses, atlantoaxial subluxation and neuromyelitis optica or Devic's disease.[8-11]

Devic's disease is characterized by acute attacks of optic neuritis and myelitis, the acute process which affects the optic nerve and the spinal cord may be simultaneous or it can be separated by weeks or months; during the acute episode of myelitis is typical to find a longitudinal involvement on the MRI images in T2 and FLAIR, and therefore the definitive diagnosis is established by the presence of anti-AQP4 with high sensitivity and specificity.[11,12]

Despite the fact that the CSF shows infectious features (bacterial or viral meningitis), is recommended to start therapy with glucocorticoids because of the benefits of their early use, while the diagnosis is confirmed, and to continue them if an infectious process is ruled out.[6] The treatment consists of the combination of 3 cycles of 1 gm of methylprednisolone intravenously and one cycle of cyclophosphamide in the acute phase, followed by oral prednisone and cyclophosphamide in monthly boluses for 3 to 12 months. The neurological response in parallel with the improvement in the MRI occurs within a few days to 3 weeks.[2,6] Relapses are common (50-60%) during the reduction of the dose of glucocorticoids, which underscores the need for maintenance immunosuppressive therapy. Plasmapheresis is used in refractory or severe cases. In the presence of positive aPL, anticoagulation therapy has good outcomes.[2,9]

Conclusion

Longitudinal myelitis is an infrequent neurological syndrome associated with SLE. However, it should be suspected in patients presenting with a clinical picture compatible with meningitis, paraparesis or paraplegia, since the prognosis depends on timely treatment. It is important to rule out the presence of aPL, in order to determine the use of antithrombotic therapy.

Ethical Disclosures

Protection of people and animals. The authors declare that no experiments were performed on human beings or animals for this research.

Data confidentiality. The authors state that patient data do not appear in this article.

Right to privacy and informed consent. The authors state that patient data do not appear in this article.

Conflict of Interest

The authors declare that they have no conflict of interest.

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