Case report

Longitudinal transverse myelitis as a clinical manifestation of Neuropsychiatric Systemic Lupus Erythematosus

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Mielitis transversa longitudinal como manifestación clínica de lupus eritematoso sistémico neuropsiquiátrico

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Abstract
Case presentation. A 22-year-old woman with a history of systemic lupus erythematosus, depression and epilepsy, allergic to hydroxychloroquine, who consulted for diarrhea, arthralgias, eyelid oedema, retro auricular pain and odynophagia. She was hospitalized for an infectious condition but requested voluntary discharge on the third day. She consulted again a week later with symptoms of ascending paraparesis, dysphagia, difficulty in urination and defecation, purplish macules on the legs, continuous fever, disorientation and psychomotor agitation. **Treatment.** She was admitted to the critical care unit. Cerebrospinal fluid, nerve conduction velocity (severe acute axonal motor polyneuropathy), and magnetic resonance imaging compatible with longitudinal myelitis were performed. **Outcome.** The patient was hospitalized for 140 days. Her evolution was monitored and physiotherapy and training for her relatives was coordinated for three days before her discharge from hospital. One month after home care, the patient was readmitted to hospital with sepsis of urinary origin and died.
Keywords
Transverse Myelitis, Lupus Erythematosus, Systemic, Autoimmune Diseases.

Resumen
Presentación del caso. Se presenta el caso de una mujer de 22 años, con antecedentes de lupus eritematoso sistémico, depresión y epilepsia, alérgica a la hidroxicloroquina, que consultó por diarrea, artralgias, edema palpebral, dolor retro auricular y odinofagia. Fue hospitalizada por un cuadro infeccioso, pero solicitó el alta voluntaria al tercer día. Regresó, una semana después con un cuadro de paraparesia ascendente, disfagia, dificultad para micción y defecación, máculas violáceas en piernas, fiebre continua, desorientación y agitación psicomotriz. **Intervención terapéutica.** Fue admitida en la Unidad de Cuidados Críticos. Se realizó estudio de líquido cefalorraquídeo, velocidad de conducción nerviosa que indica una polineuropatía motora axonal aguda severa; y resonancia magnética compatible con mielitis longitudinal. **Evolución clínica.** La paciente estuvo hospitalizada durante 140 días. Se monitoreó su evolución y se coordinó fisioterapia y entrenamiento para sus familiares durante tres días antes de su alta hospitalaria. Un mes después de recibir cuidados en casa, la paciente reingresó al hospital con un cuadro de sepsis de origen urinario y falleció.

Palabras clave
Mielitis Transversa, Lupus Eritematoso Sistémico, Enfermedad Autoinmune.

Introduction

Neuropsychiatric lupus (NPSLE) is an ongoing challenge in both diagnosis and therapeutic management. NPSLE occurs in up to 50-60 % of patients with systemic lupus erythematosus (SLE),[i] within this broad spectrum, myelopathies account for only 0.5-1 % of cases and are often associated with other neuropsychiatric disorders.[ii,iii]

Acute transverse myelitis is a potentially devastating neurological syndrome characterized by acute inflammation of the spinal cord resulting in motor, sensory and/or autonomic dysfunction. When it involves more than three spinal segments, it is referred to as longitudinally extensive transverse myelitis (LETM). Clinical presentation is variable and may manifest as lower motor neuron syndrome with flaccidity and hyporeflexia or upper motor neuron syndrome with spasticity and hyperreflexia. Up to 80 % of cases present with paraparesis, paraplegia, quadriparesis, or quadriplegia, which may even lead to the death of the patient. Approximately 70 % of cases present with autonomic disturbances such as sphincter dysfunction, bowel motility disorders, thermoregulatory abnormalities, and cardiac arrhythmias.[ii,iii,iv]

Transverse myelitis associated with systemic lupus erythematosus (SLE-TM) is a rare but serious complication of SLE, occurring in 0.5 % to 1 % of patients. However, it may manifest in up to 30-60 % of cases.[ii] Therefore, the present case was selected for description.

Generally, these tumors do not present symptoms and are incidental findings. The presence of metastatic lesions is infrequent, and there is no consensus as to the ideal management in these cases since these solid pseudopapillary tumors of the pancreas do not respond adequately to chemotherapy or radiotherapy, so surgical resection is the ideal curative treatment, even in the presence of metastatic lesions.[vi] Due to the infrequent nature of the pathology, this case is considered to be of interest, as only isolated cases have been reported.

Case presentation

A 22-year-old woman, whose primary occupation was domestic work, presented with a history of systemic lupus erythematosus (SLE) diagnosed in 2017. The patient reported a history of allergy to hydroxychloroquine and a medical history significant for depression and epilepsy, for which she had been receiving treatment with fluoxetine and carbamazepine, respectively, for the past three years. However, in 2020, she ceased her medical follow-up due to the COVID-19 pandemic. Her obstetric history included two miscarriages, one at 20 weeks and another at ten weeks of gestational age, both of which occurred in 2022.

The patient initially sought medical attention for diarrhea. She presented to the emergency department of the Rosales National Hospital with a 15-day history of generalized arthralgias, bilateral eyelid edema, profuse diarrhea, retroauricular pain, and odynophagia. She was admitted to the hospital with a diagnosis of acute gastroenteritis and received intravenous (IV) fluids and ciprofloxacin 200 mg IV every 12 hours. On the third day of hospitalization, the patient requested voluntary discharge.

A week later, the patient returned to the emergency department with a four-day history of ascending paraparesis, dysphagia, urinary and fecal retention, and the appearance of purplish macules on both legs. She also exhibited continuous fever for three days, along with one day of disorientation and psychomotor agitation.

Upon admission, the patient's vital signs were as follows: blood pressure of 107/56 mmHg, heart rate of 110 beats per minute, respiratory rate of 22 breaths per minute, and axillary temperature of 40°C. The patient exhibited symptoms consistent with hypoactivity, disorientation, and dehydration. Notable findings on physical examination included malar erythema, bilateral eyelid edema, dry mucous membranes, decreased bowel sounds, and multiple irregular purplish macules located on the distal thirds of both legs (Figure 1). The osteotendinous reflexes were graded as 3+/4 in all four extremities, and muscle strength was assessed as 3/5 in both lower limbs according to the Daniels scale.

Laboratory tests revealed non-hemolytic anemia without evidence of bleeding or melena, leukocytosis with neutrophilia, elevated transaminase levels, and nephrotic-range proteinuria, with fluctuations observed throughout the clinical course (Table 1). On May 20, 2023, a C-reactive protein (CRP) test was conducted, yielding a result of 136.65 mg/dL, which remained elevated during the course of treatment (Table 1). On May 12, 2023, the patient's C-reactive protein (CRP) levels increased to 177.51 mg/dL, accompanied by an increase in aspartate aminotransferase (AST) to 193 U/L, alanine aminotransferase (ALT) to 150 U/L, and lactate dehydrogenase (LDH) to 541 U/L.

The patient was admitted to the Critical Care Unit on April 21, 2023, where a cerebrospinal fluid (CSF) analysis was performed. The CSF sample was colorless, containing 280 red blood cells, 30 leukocytes, a glucose level of 39.7 mg/dL, and a protein concentration of 85.8 mg/dL. These findings were consistent with an infectious or inflammatory process of the central nervous system, such as vasculitis. Consequently, the patient underwent further laboratory and imaging studies. Nerve conduction studies revealed a severe acute motor axonal polyneuropathy. (Figure 2).

Treatment

Given the high suspicion of a coexisting infectious process, it was decided to initiate therapy with human immunoglobulin for five consecutive days, at a dose of 0.4 g/kg/day. Furthermore, a course of antibiotic therapy was initiated, comprising ceftriaxone 2 g IV daily and Metronidazole 500 mg IV every eight hours for a duration of three days. This was followed by piperacillin/tazobactam 4.5 g IV every eight hours until a total of ten days had elapsed. The results of blood cultures and bronchial secretion culture were negative, prompting the decision to initiate treatment with three days of methylprednisolone pulses at a dose of 1 g daily.

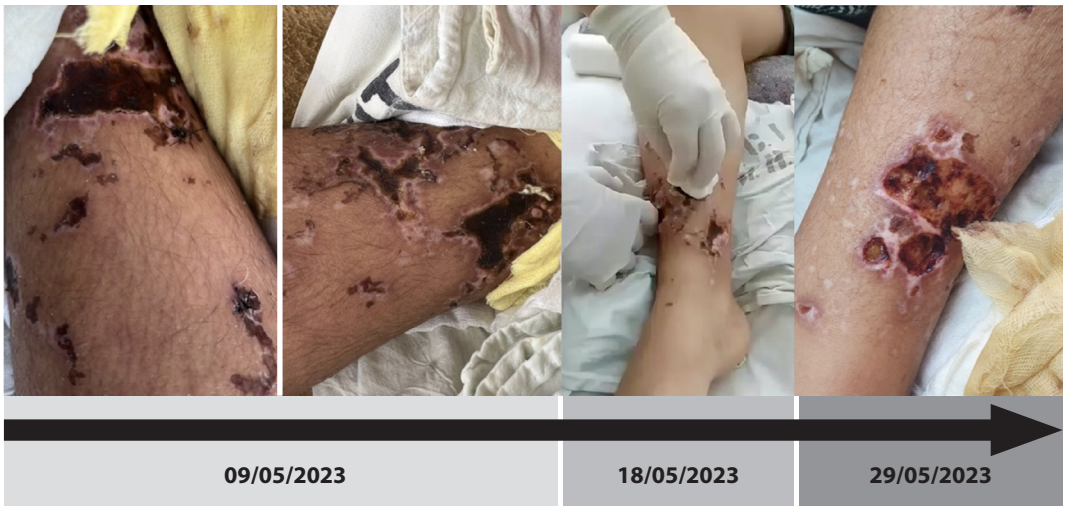

Figure 1. Evolution of macular lesions to deep ulcers from the date of admission to the intensive care unit.

Table 1. Laboratory tests throughout evolution

Date	14/04/23	26/04/23	01/06/23	12/06/23	11/07/23
Hb	13.1 g/dL	6.8 g/dL	7.2 g/dL	8.4 g/dL	9.8 g/dL
Platelets	333 000 /L	288 000/L	155 000/L	435 000/L	195 000/L
WBC	15 600/mm^3	18 400/mm^3	18 320/mm^3	21 600/mm^3	5740/mm^3
Neutrophils	12 640//mm^3	16 280/mm^3	15 720/mm^3	18 220/mm^3	3200/mm^3
Lymphocytes	1840/mm^3	1070/mm^3	2120/mm^3	2690/mm^3	2020/mm^3
Creatinine	0.81 mg/dL	0.41mg/dL	0.44 mg/dL	0.35 mg/dL	0.42mg/dL
Glucose	103 mg/dL	92 mg/dL	122 mg/dL	89 mg/dL	95 mg/dL
Total biblirubin	0.57 mg/dL	-	-	0.76 mg/dL	-
Direct biblirubin	0.19 mg/dL	-	-	0.19 mg/dL	-
Albumin	4.15g/dL	2.26g/dL	-	2.94g/dL	3.77g/dL
Others	**GUT: Protein: 15 mg/dL. leukocyte esterase 75 Leu/µL. red cells: 1xField. leukocytes: 5per Field. no casts.	Procalcitonin (central med lab):2.15 ng/m	PCR: 227.57mg/dL	PCR: 135.92mg/dL	PCR: 8.51mg/dL

*GUT: General urine test

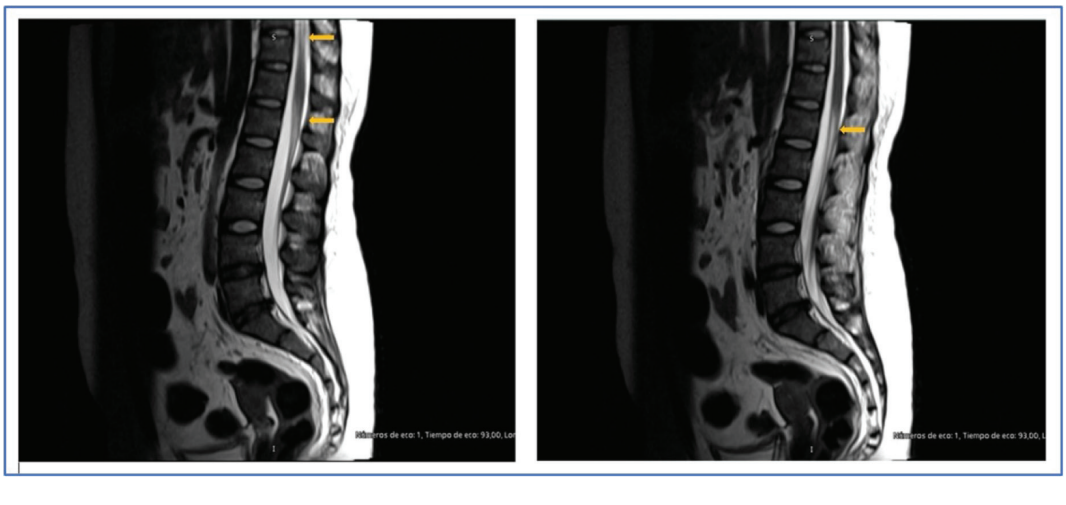

Figure 2. MRI shows hyperintense dorsolumbar spinal cord segments corresponding to demyelinating lesions involving more than three segments (T10-T11, T12-L1, and L1-L2).

Afterwards, the patient exhibited a healthcare-associated superinfection in the lower limb ulcers, caused by *Pseudomonas aeruginosa*. Consequently, glucocorticoid pulses were discontinued, and intermediate doses of hydrocortisone (100 mg every eight hours) were maintained. The administration of antibiotics was guided by an antibiogram, which revealed sensitivity to carbapenemics. This led to the completion of a ten day course of Meropenem 1 g every eight hours.

Approximately four weeks after admission to the intensive care unit and subsequent receipt of the MRI report, plasmapheresis therapy was initiated for a duration of five days.

Outcome

The patient remained hospitalized for a total of 140 days. Despite initial management with human immunoglobulin, there was no improvement in neurological manifestations or laboratory tests. Subsequent to a five-day course of plasmapheresis, the patient's condition was closely observed. This monitoring revealed the persistence of paresis in the upper limbs, paraplegia, and hyperalgesia in both legs. The patient was discharged from the hospital after three days of physiotherapy and training for her relatives. She was clinically stable.

One month after the initiation of home care and treatment, which included a daily dosage of 15 mg/day of prednisone, 100 mg/day of acetylsalicylic acid, and indomethacin administered on an as-needed basis for arthralgias, the patient continued to receive physiotherapy and assisted feeding. However, the patient was readmitted to the hospital for sepsis of urinary origin, a complication stemming from chronic bladder catheterization. The patient was treated with meropenem; however, her condition deteriorated, and she expired 72 hours after admission due to septic shock secondary to urosepsis.

Clinical diagnosis

The diagnosis was based on the clinical suspicion of a demyelinating condition associated with neuropsychiatric lupus, which was confirmed by magnetic resonance imaging.

Discussion

Demyelinating syndromes represent a minor proportion of the neuropsychiatric manifestations associated with SLE. However, following cases of trauma and infection, autoimmune diseases have been identified as the third most significant cause of demyelinating myelopathy.[iv]

The manifestation of extensive longitudinal myelitis can vary significantly, often resulting in a lower motor neuron picture characterized by flaccidity and hyporeflexia, or an upper motor neuron picture marked by spasticity and hyperreflexia.[ii] Myelitis is generally understood to be the result of a complex pathophysiological mechanism, which is typically triggered by a combination of factors, including but not limited to, trauma or infection. However, in the context of SLE, it has been postulated that its etiology may be associated with ischemia or thrombosis.[v] Despite the uncertainty surrounding the pathophysiological mechanisms, several theories have been postulated. These include dysfunction of the blood-brain barrier, de novo production of BAFF (B-cell activating factor, belonging to the TNF family) in the central nervous system, mechanisms mediated by autoantibodies (including antiphospholipid, anti-myelin, and anti/Ro antibodies), and the vascular theory (presence of vasculitis).[ii]

Myelopathies in SLE typically manifest approximately five years following diagnosis, with symptoms including fever in up to 57 % of patients, leukopenia in 48 %, and hypocomplementemia in 75 % of cases. A frequent association has been observed between the condition and antiphospholipid antibody positivity.vi In the case described, myelopathy manifested six years after diagnosis and was accompanied by fever. However, no evidence of an infectious cause was identified from the onset of symptoms until the administration of plasmapheresis.

An adequate diagnosis of transverse myelitis necessitates the performance of a nuclear magnetic resonance, which is regarded as the optimal diagnostic modality in this clinical context. This technique not only allows visualization of the spinal lesions, but also to rule out other treatable causes, such as tumors, abscesses and other lesions, helping to delimit the origin of the myelopathy.[vii] In select cases, it may also be necessary to measure specific antibodies in cerebrospinal fluid (CSF).

In this particular case, MRI revealed hyperintense T2 images at the level of the T10 T11, T12-L1, and L1-L2 segments. These findings are consistent with those reported in the extant literature. In patients diagnosed with SLE, this particular type of involvement is often characterized by its extensive

nature, which can manifest as either longitudinal or centromedullary myelitis.[vii]

Treatment of transverse myelitis in the context of SLE involves the administration of methylprednisolone pulses at a dose of 1 g/day for three days. In the absence of immunosuppression, the recommended dosage of cyclophosphamide is 0.75 1 g/m^2 body surface area, administered monthly for six months, followed by quarterly pulses of cyclophosphamide for up to two years.[viii,ix]

Plasmapheresis has been observed to be an effective option, particularly when initiated within the first 20 days from the onset of symptoms and in cases that do not respond to the use of high-dose corticosteroids.[vii] However, no change in prognosis has been demonstrated with the use of the latter therapy.[viii]

Patients diagnosed with transverse myelitis frequently experience prolonged complications. The recovery period following transverse myelitis typically commences two to twelve weeks after the onset of symptoms and can extend up to two years. However, in the absence of improvement over a period of three to six months, a substantial recovery is improbable, resulting in a range of prognoses. 1) Favorable (if recovery in 3-6 months): The treatment of young patients with early intervention has been demonstrated to yield positive outcomes. 2) Intermediate: The persistence of mild-to-moderate motor deficits has been observed. 3) Poor: patients exhibiting extensive involvement, defined as more than six segments affected, in conjunction with an inadequate response to corticosteroids or seropositivity for anti-aquaporin-4 (NMO).

Approximately one-third of individuals afflicted with transverse myelitis demonstrate a positive or complete recovery, which encompasses the restoration of ambulatory function and minimal urinary, bowel, or paresthesia-related complications. Another third exhibit moderate recovery, accompanied by persistent deficits, including spastic gait, sensory dysfunction, and substantial urinary urgency or incontinence.

The remaining third of patients demonstrate no improvement, remaining bedridden or wheelchair-bound and dependent on others for basic daily living functions. Patients who spend extended periods in bed are vulnerable to infections, the development of decubitus ulcers, and an elevated risk of deep vein thrombosis.[vi] This risk is exemplified by this clinical case in which a patient died after one month of home care due to a bladder infection. Unfortunately, there are no specific treatments to avoid or prevent these complications; however, all those related to invasive methods such as bladder catheterization can be prevented through intermittent use, prophylaxis in case of prolonged use, and adequate hygiene.[x,xiii]

In the case of extensive longitudinal transverse myelitis in a young woman, an early diagnosis or the disease is imperative. This can be achieved through MRI and lumbar puncture, which help rule out etiologies such as NMO and MOGAD.

Early treatment with corticosteroids and immunotherapy has been shown to improve prognosis; however, recovery may vary depending on the underlying cause.[ii-vi,viii-x,xiii]

Ethical aspects

The present report was formulated in accordance with the principles established in the Declaration of Helsinki and the international ethical guidelines for health-related research. Informed consent was obtained from the patient for the publication of the clinical case, thereby ensuring respect for autonomy, confidentiality, and privacy.

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