



Lupus Myelopathy in a Child

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A 5-year-old female developed, after a 7-month period of fever, anorexia, weight loss, and a transitory cutaneous erythematous eruption, a severe acute transverse myelopathy, with a partial recovery of motor and sensory function. She had positive antinuclear and antidouble-stranded DNA antibodies but no antiphospholipid antibodies. Six months later she had massive proteinuria and restarted treatment with steroids and cyclophosphamide. Our patient is one of the youngest reported with lupus myelopathy. We discuss the clinical presentation, the magnetic resonance imaging findings, and other relevant laboratory studies of this rare but serious complication of systemic lupus erythematosus. © 2002 by Elsevier Science Inc. All rights reserved.

Vieira JP, Ortet O, Barata D, Lamy S, Abranches M, Gomes JM. Lupus myelopathy in a child. *Pediatr Neurol* 2002;27:303-306.

Introduction

Systemic lupus erythematosus is a systemic autoimmune disease with frequent neurologic complications. In children the reported incidence of these complications varies from 13% to 45% [1-3].

Brain organic syndrome, psychosis, headache, movement disorders (chorea, ballismus, and ataxia), cranial and peripheral neuropathies, and myelopathy are the described neurologic manifestations of systemic lupus erythematosus [1-3].

Myelopathy, first described in 1959, is a rare complication of systemic lupus erythematosus and is particularly rare in children, with only 13 cases reported in patients

younger than 18 years of age, mostly occurring in adolescents [1,4-7].

Lupus myelopathy appears to have a stereotyped presentation in children and adults that is emerging from the published reports and includes variable time of onset of the systemic disease, acute flaccid paralysis, inflammatory cerebrospinal fluid profile with pleocytosis, raised protein and depressed glucose values, usually (but not always) positive antiphospholipid antibodies, extensive abnormality of spinal cord signal on magnetic resonance imaging, and a variable prognosis for recovery.

Our patient is one of the youngest reported with lupus myelopathy and has raised several questions regarding diagnosis and treatment.

Case Report

Our patient is a 5-year-old female, the only child of healthy, nonconsanguineous parents. She had no relevant family history, perinatal problems, or past diseases and had a normal psychomotor development.

Seven months before admission she began complaining of pain in the right lower limb, especially in the knee. Anorexia and weight loss were also present. Three months later she was presented for surgical intervention for an acute appendicitis with appendicular abscess. After surgery she suffered a prolonged intermittent febrile syndrome, lower limb pain, and a transitory diffuse erythematous rash. Three days before admission, she had a high fever, and lower limb pain worsened. Antibiotic therapy was begun while waiting for culture results for presumed urinary tract infection. She was brought to the emergency department after the acute (within a few hours) emergence of flaccid paraplegia, para-anesthesia with a D₁₀ level, and urinary retention.

She was admitted to the intensive care unit. During the next 24-48 hours her clinical condition worsened. She became tetraplegic and required ventilatory support. General examination revealed no abnormalities except for the fever, questionable nuchal rigidity, and slight dehydration. Her blood pressure was normal, no cutaneous abnormalities were apparent, and liver and spleen were not enlarged.

The child was alert and cooperative with normal mental function. Cranial nerve examination was normal. She could make movements of flexion and extension of the neck, shoulder abduction, and forearm flexion in the left upper limb, but no other movements were possible. Muscle tone was globally reduced, and reflexes were abolished except for the biceps and radial reflexes on the left side. Anesthesia, tactile, algic and thermal, was apparent up to the levels C₃ on the right and C₈-D₁ on the left. Proprioceptive sensation was difficult to evaluate although some preservation could be present.

The spinal cord magnetic resonance imaging revealed extensive multifocal areas of hypersignal in the T₁- and T₂-weighted sequences from the C₂-C₃ level down to the conus medullaris (Fig 1). Brain magnetic resonance imaging was normal. The most important laboratory findings are summarized in Table 1.

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Received November 29, 2001; accepted April 22, 2002.

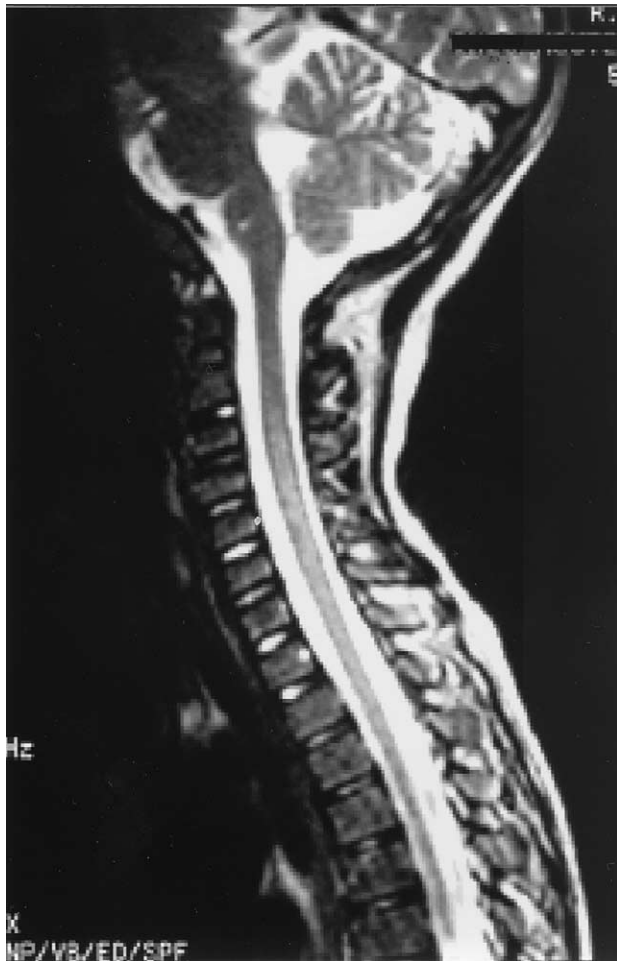


Figure 1. Cervical cord T₂-weighted magnetic resonance imaging (TR = 4,000 ms, TE = 105 ms) demonstrates edema and hyperintense abnormal signal.

The patient was initially treated with ceftriaxone, vancomycin, and dexamethasone. Therapy was changed after 3 weeks to pulses of methylprednisolone and cyclophosphamide. Assisted ventilation was

maintained for 25 days. The patient recovered normal motor and sensory function in the upper limbs, although a flaccid paraplegia and paraesthesia remained at the D₁₀ level. There was some preservation of proprioceptive sensation in the lower limbs bilaterally. She sometimes complained of abnormal sensations in the lower limbs and referred to the feeling of bladder repletion, although the pattern of bladder function reflects a probable sphincter-detrusor dyssynergia.

Spinal cord magnetic resonance imaging 12 months later revealed the disappearance of the cervical and upper dorsal cord hypersignal, but from the D₆ level and lower the cord is severely atrophic, which is more evident at the D₉ to D₁₁ level that previously demonstrated contrast enhancement (Fig 2).

Six months after the myelopathy the patient developed massive proteinuria, which required the reinstitution of steroid and cyclophosphamide treatment. Renal biopsy revealed lesions of focal and segmental proliferative glomerulonephritis.

Discussion

We consider that our patient's disease is systemic lupus erythematosus complicated with myelopathy, although we initially suggested the alternative diagnosis of an infectious or para-infectious myelopathy. A prolonged febrile disease with a rash and limb pain could be caused by several viral infections, including Epstein-Barr virus and *Cytomegalovirus* [8,9]. These agents are well-known causes of a transverse myelopathy, as well as enterovirus (coxsackievirus and ECHO virus), mumps, herpes simplex and varicella-zoster viruses, *Mycoplasma pneumoniae* and, *Borrelia burgdorferi* [8,9]. The results of the serologic studies were not compatible with these infections, however, and the positive antinuclear and anti-DNA antibodies favored the diagnosis of systemic lupus erythematosus. The late development of a massive proteinuria and glomerulonephritis are further arguments for the diagnosis of systemic lupus erythematosus as are the persistently positive ANA, anti-dsDNA, and depressed C₃ and C₄ serum levels.

Table 1. Laboratory findings in the acute phase and 2 weeks and 6 months later

Initial	Fifteenth Day	6 Months
ESR 100 mm/hr		ESR 62 mm/hr
CMV, EBV, herpesviruses, enteroviruses, <i>Mycoplasma pneumoniae</i> , <i>Borrelia burgdorferi</i> , negative bacterial cultures (blood and CSF) negative	CSF bacterial culture negative	
ANA 1/160, homogeneous pattern		ANA 1/160, homogeneous pattern
Anti-dsDNA > 50 IU/mL		Anti-dsDNA > 50 IU/mL
C ₃ , C ₄ normal		C ₃ 0.677 g/L (N:1.11–1.71)
APLAs negative		C ₄ 0.089 g/L (N:0.1–0.34)
ACLAs negative		
CSF: 600 cells/mm ³ , PMN	CSF: 32 cells/mm ³ , lymphocytes	
261 mg/dL protein	167 mg/dL protein	
43 mg/dL glucose	30 mg/dL glucose	
Proteinuria 0		Proteinuria 30 mg/M2/hr
Abbreviations:		
ACLA = Anticardiolipin antibodies	CSF = Cerebrospinal fluid	
ANA = Antinuclear antibodies	EBV = Epstein-Barr virus	
Anti-dsDNA = Antidouble-stranded DNA antibodies	ESR = Erythrocyte sedimentation rate	
APLA = Antiphospholipid antibodies	PMN = Polymorphonuclear leukocytes	
CMV = <i>Cytomegalovirus</i>		

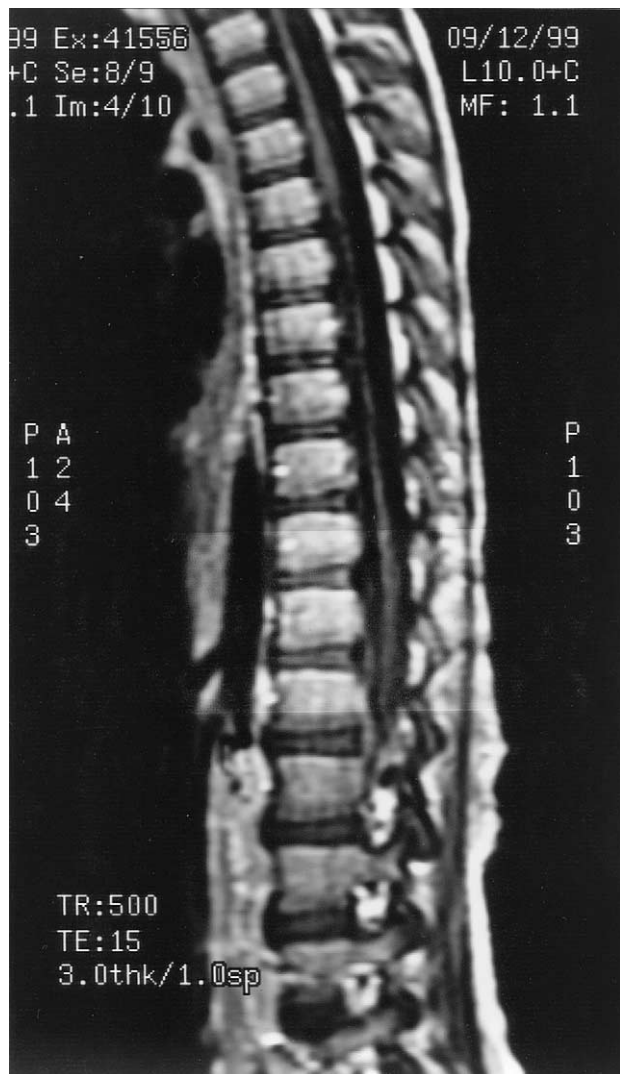


Figure 2. T_1 -weighted magnetic resonance imaging of the dorsal cord (TR = 500 ms, TE = 15 ms) exhibits a severe atrophy (12 months later).

Neurologic complications of systemic lupus erythematosus were reported in 24-51% of adults and in 13-45% of children [1-3].

Acute transverse myelitis is a rare but well-recognized complication (less than 1% of all cases of lupus; only 13 cases reported in children) [4-7]. The youngest child with systemic lupus erythematosus and myelopathy was 2 years of age at the onset of symptoms [7].

The reported cases include several patients with early onset or even as the initial manifestation of systemic lupus erythematosus [10,11]. Most patients presented with acute paraplegia, para-anesthesia, and sphincter dysfunction. The prognosis for recovery is usually guarded and may be related to prompt institution of steroid and cyclophosphamide therapy [10,11].

Many patients have antiphospholipid antibodies, and myelopathy is believed to result (in some cases) from a thrombotic vasculopathy with fibrinoid necrosis of small vessels in the spinal cord. Nomura et al. [12] reported one

14-year-old patient with acute transverse myelitis, antiphospholipid antibodies, and no clinical or laboratory evidence of systemic lupus erythematosus. Magnetic resonance imaging in this patient revealed an extensive cord lesion that did not have a vascular pattern [12].

The few reported cases with pathologic examination [13,14] reveal different types of lesions and perhaps different pathogenetic mechanisms. Some postmortem examinations revealed prominent vascular lesions (fibrinoid necrosis of arterioles and venules and perivascular lymphocytic infiltration) and myelomalacia, whereas others had surprisingly few or no vascular lesions and revealed an extensive demyelination and axonal and glial loss [13,14].

Magnetic resonance imaging in most cases revealed an extensive area of abnormal signal in the thoracic, lumbar, and sacral cord [5-7,10,15,16]. The reversibility of this abnormal signal would be more consistent with the hypothesis of demyelination, especially when a clinical recovery and resolution of the imaging abnormalities are observed.

Cerebrospinal fluid findings that demonstrate an active inflammatory process with prominent pleocytosis, raised protein levels, and depressed glucose levels also would be unlikely with a purely vascular thrombotic occlusion.

Our patient demonstrates all the above-mentioned features, including acute onset, extensive cord involvement, partial recovery, and inflammatory cerebrospinal fluid profile, although antiphospholipid antibodies were absent.

The authors would like to thank Dr. Darryl deVivo for seeing this patient and for his helpful suggestions and comments.

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