J Neurol (1995) 242:326–331

ORIGINAL COMMUNICATION

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Lupus transverse myelopathy: better outcome with early recognition and aggressive high-dose intravenous corticosteroid pulse treatment

Received: 7 February 1994
Received in revised form: 19 August 1994
Accepted: 1 September 1994

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Abstract Seven patients with transverse myelopathy (TM) were found to have systemic lupus erythematosus (SLE). Four patients had no prior diagnosis of SLE. All patients had positive antinuclear antibody (ANA). All patients had a spinal syndrome which progressed to TM with cervical or thoracic levels. The diagnosis of TM was confirmed with neurological tests and neuro-radiographic studies. Delay in diagnosis and treatment resulted in a poor outcome. Four patients died and one remained wheelchair-bound. Only two patients who received high-dose IV pulse steroid within 1 week of onset of TM had a good outcome, with full ability to ambulate without assistance. Our experience suggests that early diagnosis with early treatment using high-dose IV steroid affects the mortality and improves the outcome.

Key words Systemic lupus erythematosus · Transverse myelopathy · CNS lupus · Pulse methylprednisolone

Introduction

Transverse myelopathy (TM) may occur as an uncommon manifestation of systemic lupus erythematosus (SLE) [1–7]. Previous case reports established the severity and poor prognosis of this syndrome [1, 2, 7]. Recent reports have suggested a better outcome in response to intravenous (IV) methylprednisolone and cyclophosphamide pulse treatment [8–11]. At the University of Mississippi Medical Center (UMC), we found seven patients with TM due to SLE between 1975 and 1990. We reviewed their diagnostic and clinical features, treatment and outcome retrospectively. In a preliminary report, we concluded that early recognition and aggressive treatment with a high dose of IV corticosteroid could lead to a better outcome [12].

Patients and methods

From January 1975 to December 1990, 424 patients were admitted to UMC with the coded diagnosis of SLE. Of these 424 patients, nine also had a diagnosis of myelopathy. Review of these nine record revealed that one patient had neurosyphilis, and another had coexisting subacute combined degeneration of the spinal cord confirmed by autopsy. The remaining seven patients were included in this study of TM secondary to SLE. All patients were seen by a rheumatologist (V.H.). The diagnosis of TM was made by the neurologists (D.D., S.H.S.), based on appropriate clinical features, including paraparesis or quadriparesis, with or without a sensory level and sphincter dysfunction. Confirmation of the diagnosis was based on studies of cerebrospinal fluid (CSF), EMG nerve conduction studies, and imaging procedures such as CT, myelography, or MRI. In all seven cases, infections, metabolic disorders, and malignancy were ruled out.

Results

All patients were female; their ages ranged from 16 to 52 years with a mean and standard deviation of 34.7 and 13.2 years. All patients had positive antinuclear antibody (ANA). Only two patients had a previous diagnosis of SLE prior to the onset of TM. One patient had a previous diagnosis of discoid lupus. The remaining four patients were first diagnosed as having SLE when admitted for TM. Diagnosis of SLE was made in two of the four pa-

Table 1 Association of transverse myelopathy *(TM)* with systemic lupus erytheratosus *(SLE)*: clinical summary and physical findings

Patient	Age at onset of TM (years)	SLE criteria	Duration of SLE prior to TM	Constitutional symptoms	Neurological symptoms	Physical findings
1	45	Facial rash ANA 1:640 Anti-DS-DNA = 14 CNS involvement	Simultaneous Diagnosis of SLE delayed for 1 month	Nausea and vomiting for 3 weeks	Rt. hemiparesis followed in 3 days by Lt. hemiparesis	Quadriparesis with brisk reflexes, extensor plantar responses, saddle anesthesia, incontinence
2	52	Arthralgia Discoid rash ANA 1:520 Anti-DS-DNA = 1.6 (mildly elevated) CNS involvement	Diagnosis of discoid lupus for 10 years Diagnosis of possible SLE 3 months prior to TM	None	Ascending paresthesias, inability to walk and difficulty voiding within hours	Quadriparesis with severe weakness in legs, severely impaired vibratory sense, no sensory level to pain, temperature, brisk reflexes, extensor plantar responses, reduced rectal tone
3	16	ANA 1:700 Anti-Smith 1:200 Anti-RNP pos. Anti-DS-DNA = 71.9 CNS involvement	Diagnosis of SLE delayed for 3 years after onset of TM	None	Rt. arm and leg paresthesia, weakness progressing to quadriparesis	Marcus Gunn pupil, paraplegia with sensory level at T3, urinary incontinence
4	25	ANA 1:640 Focal proliferative glomerulonephritis Arthralgia CNS involvement	Simultaneous History of arthritits, 3 years prior to TM	Fever to 104°F (40°C)	Dimming of vision, Rt. eye, followed by inability to move both legs	Paraplegia, T2 sensory level, RT. Marcus Gunn pupil with optic atrophy, urinary incontinence
5	25	Hemolytic anemia Pleural effusion False + VDRL CNS involvement	4 years	Influenza-like symptoms, malaise, low-grade fever, tight sensation in chest	Paraplegia over 24 h with incontinence and urinary retention	Quadriparesis, absent reflexes, flacid sphincter, incontinence
6	45	Pleural effusion Pericardial effusion ANA 1:200 CNS involvement	1 year	None	Tingling paresthesia of legs followed within 12 h by inability to move legs	T5 sensory level, flacid paraparesis with weakness in both upper extremities, reflexes absent in legs, 1 to 2+ arms, urinary incontinence
7	35	ANA 1:320 Anti-DS-DNA = 8.7 CNS involvement	Simultaneous	Frontal headache	Rt. hemiparesis	4/5 muscle strenght on Rt. arm and leg, absent sensation below the neck on Rt., brisk reflexes, extensor plantar responses, normal sphincter control

tients during their initial presentation of TM but was delayed by a month in one patient and delayed by 3 years in the other patient (Table 1).

Six patients had at least 4 of the 11 criteria for the diagnosis of SLE according to the 1982 ACR classification criteria [13]. One patient with acute TM had no other clinical disease related to SLE but had a positive ANA and elevated antibodies to DS-DNA (Table 1).

Neurological symptoms began acutely, often with paresthesias which rapidly evolved into paraplegia and often quadriplegia (Table 1). The evolution of neurological deficits occured within a few hours, with four of the seven patients progressing to maximum deficit within 48 h. Two patients (nos. 2,5) became quadriparetic; patient 6 developed T5 paraplegia and patient 7 had right hemiparesis. Three patients took longer than 48 h to evolve into maxi-

Table 2 Results of neurological investigations, treatment and outcome (*DMS* dexamethasone, *MP* methylprednisolone, *UMC* University of Mississippi Medical Center)

Patient	CSF findings	CT	MRI	Treatment	Outcome
1	Day 4, WBC = 3 RBS = 127 glucose = 57 protein = 66 Day 40, WBC = 10 (20% S, 80% L) RBC = 12 glucose = 48 protein = 332 Normal IgG index, Absent oligoclonal bands	Day 3, Brain, cervical spines radiographs – within normal limit (WNL)	Day 6, Brain stem and spinal cord WNL Day 40, spinal cord enhancing lesions, C3 through C7	Day 53, pulse IVMP, 1 g daily × 3, IV DMS, 6 mg q 6 h Discharged day 103 on prednisone 20 mg p.o. q.d.	Died 6 months after onset from sepsis
2	Day 6, WBC = 48 (100% L) RBC = 110 glucose = 60 protein = 44	Pan myelogram with CT-enlarged cord C5 through C7	Not done	Day 6, IV DMS, 50 mg follwed by 10 mg q 6 h Day 9, IVMP, 125 mg q 4 h plus IVMP, 1g daily × 3 Day 12, prednisone, 60 mg p.o.q.d. Day 29, prednisone, 40 mg p.o.q.d. Discharged, day 39	Able to ambulate without assistance on discharge
3	3 months, WBC = 7 MS panel = neg.	Brain and cervical spines WNL	3.5 years Brain-cerebral nonperi-ventricular plaques	1st week DMS p.o. dose unknown, referred to UMC 3 years after onset, prednisone, 60 mg p.o.q.d Discontinued by patient after 1 week	Died 6 years after initial onset
4	Day 7, WBC = 17 (1S, 16 L) RBC = 0 glucose = 67 protein = 46 IgG = 19.4 VDRL = neg.	Myelogram – WNL	Not done	1st week – prednisone 60 mg p.o.q.d. for 2 months dose tapered to 50 mg p.o.q.d.	Died 5 years after onset
5	Day 8, WBC = 450 (86% S, 14% L) protein = 950 glucose = unknown Day 13, WBC = 22 (20% S, 80% L) RBC = 0 glucose = 39 protein = 29	Day 8, myelogram – T5 lesion	6.5 years, spinal cord – abrupt reduction in cord diameter at C7, extended caudally 4 vertebral segments, consistent with myelomalcia	Day 12, DMS, 5 mg p.o. q 6 h with slow tapering Discharged day 34 on DMS, 5 mg p.o.q. 12 h	Paraparetic, able to learn wheelchair transfer at time of discharge
6	Day 21, WBC = 18 (100% L) RBC = 4 glucose = 106 protein = 41 MS panel = neg.	Day 21 myelogram – no block Post-myelogram CT-small punctate areas of T4 to T8 (myelomalacia)	Day 19, spinal cord – increased signal on T1 and T2 images at upper-mid thoracic levels extending up to lower cervical regions Day 20 , brain – (uncontrasted) bilateral thalamic lacunes and left inferior temporal lobe infarct	Day 27, pulse IVMP, 1 g daily × 3 Day 47, pulse IVMP 1 g daily × 3	Died in post-operative period 2 months after onset
7	Day 8, WBC = 26 (90% L, 10% M) RBC = 0 glucose = 66 protein = 59	Day 2, brain (with and without contrast) – WNL Day 7, brain – WNL	Day 3, spinal cord – bright T1 signal, right hemi- cord C2 to C5 Day 6, spinal cord with gadolinium – C2 to C5 cord fusiform enlargement with increase signal Day 18, spinal cord – C2 to C7 right hemicord abnormal T2 signal	Day 6, IV DMS, 10 mg q 6 h Day 8, pulse IVMP, 1 g daily × 3 Day 11, prednisone, 40 mg p.o.b.i.d. with slow tapering Day 42, prednisone, 50 mg p.o.q.d. Patient discontinued prednisone after 1 week	Ambulating without assistance within 2 weeks of onset. Relapse after discontinuing medication. Recovered again with pulse IVMP, 1 g daily × 3 within 1 week

mum neurological deficit. Patient 1 became quadriparetic; patients 3 and 4, paraplegic with unilateral optic neuritis. Three patients had constitutional symptoms including nausea, vomiting, malaise and fever.

All patients underwent imaging studies of the spinal cord (myelogram and MRI) to rule out compressive lesions. Imaging of the cord with myelography either showed no lesion or diffuse enlargement of the cord at the appropriate level (Table 2). Three patients had MRI of the spinal cord during the acute phase of the myelopathy. Typically, intramedullary lesions with increased signal intensity on T2-weighted images, extending through several segments, were seen. These lesions enhanced with gadolinium in patient 7. MRI 6.5 years after the onset of TM in patient 5 showed an atrophic spinal cord. CSF typically showed a modest pleocytosis with predominantly mononuclear cells and either normal or mildly elevated protein values. Patient 5 with a subarachnoid block due to a swollen cord had a protein level of 950 mg%.

A summary of treatment and outcome is shown in Table 2. Patient 1 received pulse steroid with intravenous methylprednisolone (IVMP), beginning on the 53rd day after the onset of TM. No improvement was seen in her neurological symptoms. She had persistent C5 level quadriplegia and died 6 months later from urinary tract sepsis. Autospy revealed perivascular infiltrates, inflammatory cells, and liquefactive necrosis of the cervical cord.

Patient 2 was treated promptly with IV dexamethasone (DMS), 50 mg beginning on day 6 after the onset of TM followed by 10 mg every 6 h. IVMP, 1 g daily was given for 3 days from day 9 through 11 while she received IVMP, 125 mg every 4 h. She made a complete neurological recovery and was discharged home on day 39, walking without assistance.

Patient 3 was referred to UMC 3 years after the onset of TM. Initially, she was treated by her local physician with an unknown dose and duration of oral DMS. Prednisone, 60 mg daily was given but the patient discontinued taking it 1 week later. She was followed in the lupus outpatient clinic with stable T3 paraplegia and bladder incontinence. Three years later (6 years after the onset of TM), the patient relapsed with quadriplegia and diaphragmatic paralysis and died of urinary tract sepsis.

Patient 4 received only oral prednisone, 60 mg daily for 2 months with tapering thereafter. Improvement of strength was slow and the patient remained weak. She died at home of unknown causes 5 years after the onset of TM.

Patient 5 had a laminectomy at the T3–T6 level on day 10, which revealed arachnoiditis. Treatment with oral DMS, 5 mg every 6 h was started on day 12. She remained paraparetic with about 65% function of the lower extremities, and was discharged home with use of a wheelchair and self-catheterization. Six and a half years after the initial onset of TM, she had a relapse with total paralysis of the lower extremities and weakness of the right arm. IVMP, 1 g daily for 3 days was given and resulted in rapid improvement of muscle strength in the right upper extremity. She remains wheelchair-bound and requires self-catheterization, but her neurological condition remains stable on maintenance treatment with prednisone 5 mg and hydroxychloroquine 200 mg daily, 11 years after the initial onset of TM.

Patient 6 was transferred to UMC 19 days after the onset of TM. Pulse IVMP was started at 1 g daily on day 27 for 3 consecutive days. No improvement was seen after treatment. A second course of pulse IVMP was given on day 47. The patient developed ischemic bowel necrosis with sepsis and died in the postoperative period.

Patient 7 was treated on day 6 with IV DMS, 10 mg every 6 h followed by IVMP, 1 g daily for 3 days beginning on day 9. She recovered promptly and walked without assistance within 2 weeks of onset. The patient was discharged on prednisone 50 mg daily but chose to stop it 1.5 months later. She had a relapse of right Brown-Sequard syndrome with extension into the bilateral dorsal columns. IVMP 1 g daily for 3 days was promptly given and she recovered again with complete resolution of weakness. Subsequently, she was lost to follow-up.

Discussion

Only two of our seven patients (nos. 5 and 6) had a previous diagnosis of definite SLE, 1 year and 4 years prior to the onset of TM. Diagnosis of SLE in all five patients without a history of SLE was made during evaluation by the rheumatologist. Six patients fulfilled at least four criteria of the ACR classification [13]. Patient 3 had no other clinical symptoms of SLE but had high titre ANA, speckled pattern, positive anti-Smith at 1:200 titre, positive anti-RNP (anti-ribonucleoprotein) and anti-DS-DNA.

In our series of patients, the onset of TM ranged from 3 months to 4 years after the onset of SLE but was simultaneous in three of the seven patients. Only three patients had a late onset of TM 1 year or later after the onset of SLE. In the review by Andrianokos et al. [2], the onset of TM was more often late during the course of SLE. However, the finding of TM as a presenting symptom of SLE or as an early feature of SLE was also not uncommon [2, 3]. Nine of 23 patients reviewed by Andrianokos et al. had no previous diagnosis of SLE. Seven of the nine patients in their review also had symptoms of SLE in other organ systems. Five of our seven patients with TM had inactive SLE in other organs. Patient 4 had evidence of lupus nephritis. Patient 2 was taking maintenance steroids for polyarthralgia during the onset of TM. A review of CNS manifestations in SLE by Sibley et al. [14] showed that 81% of CNS symptoms occurred in the absence of other SLE exacerbations.

Presenting symptoms in our patients included paresthesia in three, influenza-like illness with low grade fever in one, high fever (104° F, 40° C) in one, right hemiparesis

in one, and right hemiparesis with headache in one. Fever is common at the onset [2]. Bilateral leg numbness and weakness or tingling paresthesia are the most common presenting symptoms [2]. Interscapular pain, low back or abdominal pain are occasionally seen [2]. Urinary retention is also common [2].

The progression from initial symptoms to maximum deficit occurred over 12 h to 1 month in our patients. In the review by Ropper and Poskanzer [15], 28 of 36 patients with a progressive course of acute TM stabilized to a maximum deficit in 1–10 days; 3 patients in 12–24 h, and 4 patients in 10–14 days. None of our patients had the hyperacute catastrophic onset described in 11 patients of Ropper's series. However, they reviewed acute transverse myelitis from all etiologies.

Two of our patients had spinal shock with absent reflexes. One survived with no improvement of her deficit. The other had no improvement and died 74 days after the onset of TM. One large study of TM of all etiologies revealed that spinal shock correlated with a poor outcome [16]. Of our five patients with preserved reflexes, two experienced nearly complete recovery.

SLE patients with TM had a poor prognosis. Of 26 cases described and reviewed by Andrianokos et al. [2], 13 patients died, 9 had permanent neurological deficits and only 4 recovered with nearly normal function. Review by Warren and Kredich [3] showed that in spite of prednisone therapy, 10 of 30 patients died within 6 weeks of diagnosis of TM. Steroid treatment appeared to be more effective if started within 24 h of onset of TM. High-dose IVMP, 250 mg every 6 h was used by Warren and Kredich to treat a 14-year-old girl with lupus encephalopathy and myelopathic syndrome. Complete recovery from myelopathic symptoms was achieved within 1 week of treatment. Aggressive treatment with IVMP alone [3, 8, 9] or in combination with IV cyclophosphamide resulted in improved outcome [10, 11]. In the series reported by Barile and Lavalle [11], of seven SLE patients with TM treated with IVMP and IV cyclophosphamide, five were able to walk, three had either total or adequate sphincter control, two had neurogenic bladder, one was confined to a wheelchair with partial sphincter control, and one did not respond to treatment and died of pulmonary embolism.

In our retrospective review, diagnosis was delayed in patients 1 and 6 due to late referral. In spite of IVMP treatment, beginning on day 27 and day 53, both patients failed to improve and both died by the sixth month. Three other patients received oral steroids early in the course of their TM, but remained paraparetic, wheelchair-bound and had neurogenic bladder. Of these three patients, one patient (3) died 4 years later at home of an unknown cause; patient 4 died during a relapse 6 years after the initial onset of TM. The third patient was alive after surviving a second episode of TM but recovered to baseline after IVMP therapy. Only two patients in our series who received high-dose steroid as IVMP or IV DMS beginning on the 6th day after onset of TM recovered with complete motor and sphincter function. We agree with others that early recognition of TM due to SLE with early treatment using IV steroid affects the mortality and improves the outcome. Although IV cyclophosphamide was not used in our series, it should not be withheld if recovery is slow or incomplete following IVMP, and there are no major risk factors for fatal infection.

In summary, we have presented our clinical observations on seven patients with SLE and TM, showing that outcome in these patients is poor if diagnosis and aggressive treatment are delayed. Two patients in our series treated with IVMP within the 1st week after onset had a better outcome. Although our experience is limited, we agree with Barile and Lavalle [11] and Boumpas et al. [10] that aggressive therapy should be used in SLE patients with TM because if treatment is delayed or inadequate, the prognosis is extremely poor with permanent disability or death.

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