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CASE REPORT

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Catastrophic transverse myelitis in a patient with systemic lupus erythematosus

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Abstract A 24-year-old Japanese woman was admitted to our hospital suffering from high fever and progressive paralysis in both legs. Magnetic resonance imaging of the spinal cord showed high-intensity signals from C5 to Th4 and from Th7 to L1 on T2-weighted images. The patient was diagnosed as having acute transverse myelitis (TM), which was a complication of systemic lupus erythematosus based on the serological findings. Despite aggressive immunosuppressive treatments including corticosteroid pulse therapy, plasmapheresis, and intravenous cyclophosphamide, the paralysis of her lower extremities did not improve. In the catastrophic type of lupus-associated TM, which develops extensively and longitudinally along the spinal cord, the prognosis still seems to be poor despite intensive treatments.

Key words Intravenous cyclophosphamide (IV-CY) · Systemic lupus erythematosus (SLE) · Transverse myelitis (TM)

Introduction

Transverse myelitis (TM) is a rare but serious complication of systemic lupus erythematosus (SLE).[1] The pathogenic mechanism of TM is still speculative, and no optimal management strategy has yet been established.[2] Recent reports indicate that early aggressive therapy including high-dose steroids and cytotoxic agents is associated with a satisfactory outcome.[3] However, overall prognosis of SLE patients with TM is not always favorable.[4] We describe a female patient having lupus-related TM with the extensive involvement of longitudinal spinal segments. Although prompt corticosteroid pulse therapy plus plasmapheresis and intravenous cyclophosphamide (IV-CY) suppressed the serological activity of SLE, these treatments did not resolve her neurological involvement completely.

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Case report

A 24-year-old Japanese woman presenting with high fever was transferred to our hospital for further examinations. She was initially admitted to a local hospital for polyarthralgia, high fever, appetite loss, and general fatigue. On admission day she had progressive paresthesia in her lower limbs. Ten hours after admission, she recognized bilateral loss of strength and sensory activity in her lower extremities, and difficulty in controlling the vesicle sphincter. On physical examination, her consciousness was clear and her vital signs were as follows: body temperature 38.8°C, blood pressure 108/68 mmHg, heart rate 57 beats/min, respiratory rate 16/min. Neurological findings revealed sensory paralysis on the Th12–L3 area on both sides and motor paralysis of the bilateral lower extremities. Bilateral patellar tendon reflex had disappeared. There was no skin lesion including face erythema. Her bilateral wrist joints were swollen. In blood cell analysis and biochemistry analysis (Table 1), lymphocytopenia (503/mm^3) and hypoalbuminemia (3.2 g/dl) were observed. In serological analysis, antinuclear antibody was positive (×1280, diffuse), and anti-dsDNA (299 IU/ml) and anti-Sm (36.6 IU/ml) antibodies were elevated. Hypocomplementemia (CH_{50} 6 IU/ml, C3 33 mg/dl, C4 6 mg/dl) was also observed. Although lupus anticoagulant and anti-β2GPI antibody was not detected, anticardiolipin IgG antibody was positive in low titer (11.9 IU/ml). A lumbar puncture revealed white blood cell

Table 1. Laboratory data on admission

Peripheral blood		Blood chemistry	
RBC	3.81×10^6/μl	Na	137 mEq/l
Hemoglobin	11.1 g/dl	K	3.3 mEq/l
Hematocrit	32.3%	Cl	102 mEq/l
WBC	7500/μl	IP	2.7 mg/dl
Baso	0.9%	Ca	8.1 mg/dl
Eosino	0%	BUN	8.2 mg/dl
Neutro	86.3%	Cr	0.4 mg/dl
Lymph	6.7%	TP	6.9 g/dl
Mono	6.1%	Alb	3.2 g/dl
Platelet	16.7×10^4/μl	T.Bil	0.5 mg/dl
ESR	48 mm/h	AST	26 IU/l
Urinalysis		ALT	40 IU/l
Specific gravity	1.02		
Protein	30 mg/dl		
Occult blood	2+		
Serological examination			
CRP	0.34 mg/dl	Anti-dsDNA Ab	299 U/ml
IgG	1986 mg/dl	Anti-SS-A Ab	21.9 U/ml
IgA	372 mg/dl	Anti-SS-B Ab	≤7.0 U/ml
IgM	180 mg/dl	Anti-Sm Ab	36.6 U/ml
MPO-ANCA	(−)	Anti-RNP Ab	46.6 U/ml
PR3-ANCA	(−)	C3	33 mg/dl
Anti-β2-GP1Ab	≤1.2 U/ml	C4	6 mg/dl
ANA	×1280	CH_{50}	5 U/ml
LE test	(+)	IC	5.3 μg/ml
Anticardiolipin antibody	11.1 U/ml	Lupus anticoagulant (dRVVT)	(−) 1.18 (<1.20)
CSF			
PH	7.2	Protein	210 mg/dl
Cell count	2004/mm^3	Sugar	22 mg/dl
Poly	53%	Oligoclonal band	(−)
Mono	47%		

RBC, red blood cells; WBC, white blood cells; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; MPO, myeloperoxidase; Ab, antibody; ANCA, antineutrophil cytoplasmic antibody; ANA, antinuclear antibody; IC, immune complex; CSF, cerebrospinal fluid; anti-β2-GP1Ab, anti(cardiolipin)β2–glycoprotein I complex antibody

counts of 2004 cells/mm^3 (47.1% neutrophils, 53.1% lymphocytes). Protein was 210 mg/dl and glucose 22 mg/dl. Cerebrospinal fluid cultures were negative for microorganisms, and there was no oligoclonal band. Magnetic resonance imaging (MRI) of the brain and spine revealed high-intensity signals on medulla oblongata and at the levels from C5 to Th4 and Th7 to L1 (Fig. 1). Based on the laboratory data and MRI findings, the patient was diagnosed as having acute TM as a complication of SLE. On the day of admission, we started methylprednisolone pulse therapy for 3 days, followed by oral administration of prednisolone (50 mg/day). High fever and severe neuralgia at the Th4–Th8 levels improved under this treatment. However, the motor palsy of her lower extremities did not change. Therefore, plasmapheresis (twice per week, a total of four times) synchronized to steroid pulse therapy was additionally performed. At hospital day 14, intravenous cyclophosphamide (IV-CY, 500 mg/day) therapy was combined with oral steroids. After the second round of IV-CY therapy, the patient experienced macrohematuria and this therapy was abandoned. Although a repeat MRI scan of the spinal cord showed resolution of the high-intensity signals on the medulla oblongata (Fig. 1A) and at the C5–Th1 levels (Fig. 1B), the high-intensity signals from Th10 to L1 persisted (Fig. 1C). Three months later, serological findings including hypocomplementemia and elevated anti-dsDNA antibodies were normalized under these treatments. However, bilateral paralysis and sensory loss of the lower extremities remained.

Discussion

We experienced a case of TM in association with SLE. In our patient, TM developed rapidly as the first manifestation of SLE and extensively affected the longitudinal spinal cord. We considered this case as catastrophic TM in association with SLE. Transverse myelitis is a rare but serious complication of SLE.[5] Although the exact pathogenic mechanism of TM in SLE has not yet been elucidated, vasculitis, antibodies to neural cells, and the deposition of immune complex (IC) are thought to contribute to this serious complication.[6] The optimal treatment strategy is unclear and the overall prognosis has not been associated with a better outcome. It has been postulated that aggressive treatment early in the

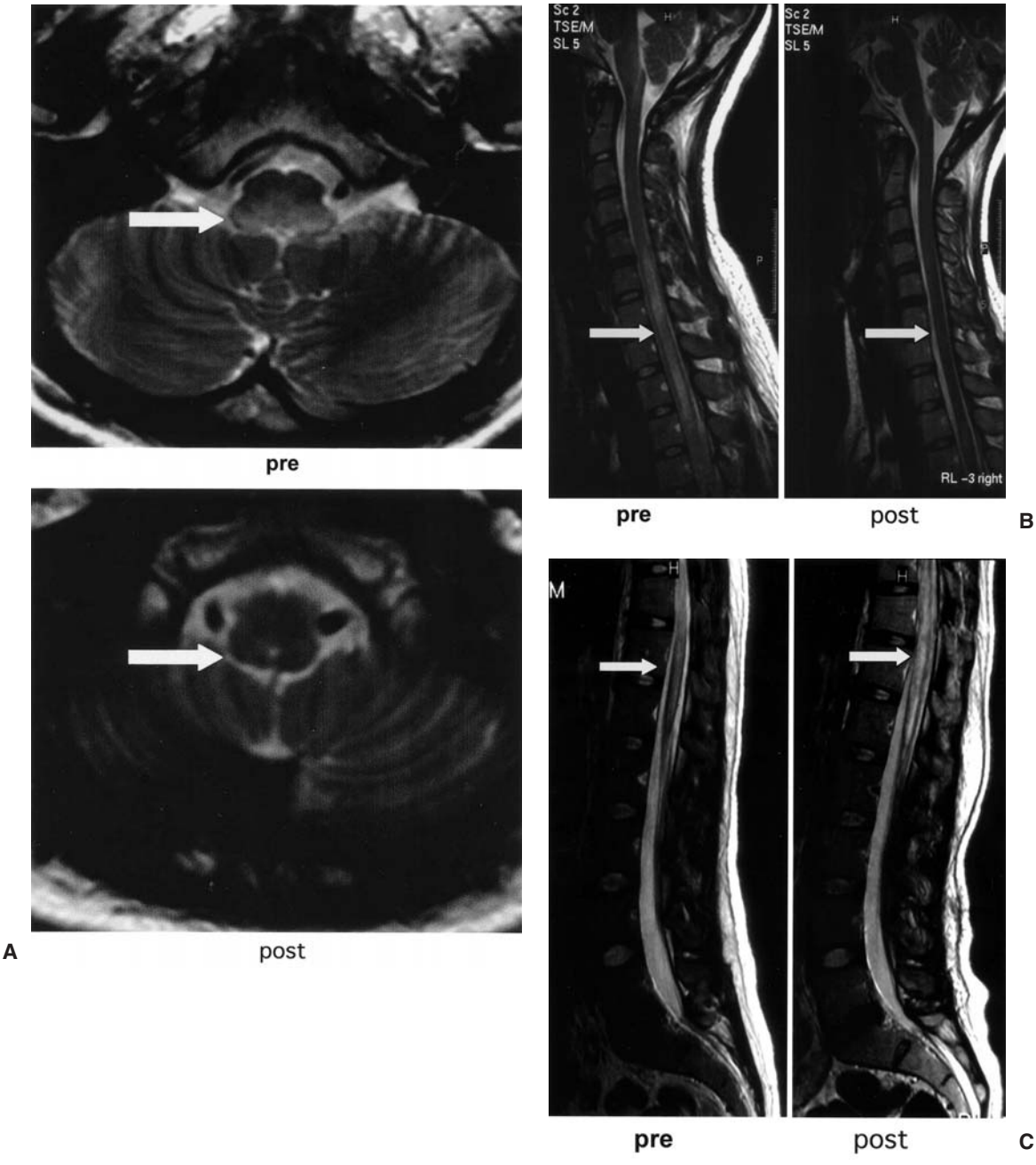

Fig. 1. **A** T2-weighted magnetic resonance image (MRI) on admission (*pre*) demonstrating the increased signal intensity of the medulla oblongata (*arrow*). These abnormal signals completely resolved after administration of steroid pulse and intravenous cyclophosphamide (IV-CY) therapies (*post*). **B** T2-weighted MRI on admission (*pre*) demonstrating the increased signal intensity of the cervical spinal cord (*arrow*). These abnormal signals completely resolved after administration of steroid pulse and IV-CY therapies (*post*). **C** T2-weighted MRI on admission (*pre*) demonstrating the swelling and increased signal intensity of the lower thoracic and sacral spinal cord (*arrow*). These abnormal signals did not resolve after administration of steroid pulse and IV-CY therapies (*post*)

course of the disease is critical for a favorable response.[7] There are no therapeutic guidelines for TM in SLE. Recent reports suggest that early treatments with high-dose corticosteroid and intravenous cyclophosphamide (IV-CY) may improve neurological involvement in SLE patients with extensive TM.[3] Notably, however, according to a review of lupus-related TM, complete recovery occurred in 50%, partial recovery in 29%, and no improvement was observed in 21% of patients.[4] Therefore, the overall outcome of TM is still poor. The prognosis seems to depend on factors such as rapid diagnosis, extent of the neurological involvement, and promptness of treatments.[8]

In our case, hyperacute and longitudinal TM was confirmed by MRI images. We started steroid pulse therapy and synchronized plasmapheresis promptly around the time of admission, and IV-CY was combined with the basal steroid therapy. These treatments rapidly suppressed SLE disease activity, and the high-intensity signals and swelling of C5–

Table 2. Treatment and outcome of patients with systemic lupus erythematosus and transverse myelitis

First author (year)[Ref.]	No. of patients	Treatment		Outcome	
Barrile (1992)[3]	7	PSL+IV-CY	7	CR	2
				PR	4
				N	1
Mok (1998)[2]	10	PSL	1	CR	4
		PSL+AZA	3	PR	5
		PSL oral CY	4	N	1
		PSL+IV-CY	2		
Kovacs (2000)[4]	14	PSL	5	CR	3
		PSL+IV-CY	6	PR	2
		PSL+IV-CY+PE	3	N	9
Kovacs (2000)[4] (Review)	91	?		CR	50%
				PR	29%
				N	21%
Cruz (2004)[12]	15	PSL	2	CR	3
		PSL+IV-CY	2	PR	11
		PSL+IV-CY+AZA	10	N	1
		PSL+AZA	1		

AZA, azathioprine; CR, complete recovery; CY, cyclophosphamide; IV-CY, intravenous cyclophosphamide; PR, partial recovery; PSL, prednisolone; N, no improvement or deterioration

Th1 spinal cord disappeared. However, the high-intensity signal at the Th10–L1 levels did not change and the paralysis of both lower extremities was not reversible. In the thoracic region of the spinal cord, the blood supply is thought to be limited. The longitudinal arterial trunks are largest in the cervical and lumbar regions and much smaller in the thoracic lesions.[9] It is possible that this circulatory disturbance may contribute to the poor response of this region to treatment.

Recently, Kimura et al.[10] reported a case of lupus-associated TM in which the patient did not respond to aggressive treatment including corticosteroid pulse therapy, IV-CY, and plasmapheresis. They suggested that any vasculopathy in addition to the autoimmune mechanism contributes to the pathogenesis of refractory lupus-associated TM. Lavelle et al.[11] also reported a strong association between acute TM and antiphospholipid antibodies, and suggested that the ischemia due to thrombosis or vasculopathy is related to the course of TM. In our patient's case, TM presented as the initial symptom of SLE and extensive longitudinal lesions of the spinal cord were demonstrated. The hyperacute and catastrophic type of lupus-associated TM appears to be refractory to various immunosuppressive treatments. Recent studies investigating the treatments for SLE-related TM are summarized in Table 2. Early aggressive therapies using a combination of corticosteroids and cytotoxic agents may be superior to corticosteroids alone. However, the complete recovery rate is still less than 50%.[12] Further study is needed to establish the optimal treatment for this rare and serious complication of SLE.

We tentatively conclude that the catastrophic type of TM could occur in a subset of SLE patients, and that conventional immunosuppressive treatments may be insufficient to control this serious complication. New immunosuppressive therapies, including rituximab, which has been shown to be effective for refractory central nervous system SLE,[13] should be evaluated to delineate the best treatment strategy to induce complete recovery.

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