Sporadic Amyotrophic Lateral Sclerosis Showing Abnormal Somatosensory Evoked Potentials : A Report of Three Cases

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Sporadic Amyotrophic Lateral Sclerosis Showing Abnormal Somatosensory Evoked Potentials : A Report of Three Cases

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Abstract *Objective*-Although dysfunction of the sensory systems in sporadic amyotrophic lateral sclerosis (ALS) has been reported, the clinical characteristics of such cases still remain unknown. We therefore performed a clinico-electrophysiological analysis of sporadic ALS patients. *Material and methods*-Twelve ALS patients (aged 36-66 years), who had their somatosensory evoked potentials (SEPs) evaluated, were reviewed and their clinical characteristics were delineated. In addition, needle EMG, sensory nerve conduction velocities, motor evoked potentials (MEPs) and cervical MRI or plain X-ray of the neck were also recorded. *Results*-Three cases were segregated from the other 9 patients because of predominant upper motor neuron signs with pseudobulbar palsy and abnormal posterior tibial nerve and/or median nerve SEPs. The MEPs were also abnormal in these 3 patients and the brainstem auditory evoked potentials were abnormal in one patient. EMG revealed less involvement in the lower motor neurons. *Conclusion*-Sporadic ALS with a predominant upper motor neuron sign and also demonstrating pseudobulbar palsy with abnormal SEPs, may therefore form a clinical subtype of ALS.

Key words : amyotrophic lateral sclerosis, pseudobulbar palsy, subclinical sensory involvement, somatosensory evoked potentials, motor evoked potentials

1. Introduction

Amyotrophic lateral sclerosis (ALS) is a degenerative disease of the upper and lower motor neurons. It is characterized by progressive weakness and amyotrophy of the limb, trunk, and/or bulbar muscles in the absence of sensory or autonomic disturbances. Pathological findings usually show a degeneration of only the pyramidal tracts and anterior horn cells, but involvement of sensory system has been reported[4)13)19)]. Somatosensory evoked potential (SEP) studies have also suggested the involvement of the sensory pathways in some pateients with this condition[2)8)14)]. Most cases are familial, but some authors have also reported sporadic cases of ALS which might be multisystemic including the posterior column[1)3)12)]. However, the clinical manifestations of such sporadic ALS cases with abnormal SEPs have not yet been characterized in detail. We herein report 3 cases accompanied with abnormal SEPs. These patients were clinically distinct from 9 other typical ALS patients.

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2. Patients and methods

2.1. Patients

Twelve patients (4 males and 8 females) were diagnosed to have ALS between June, 1993 and September, 1997 at Kyushu University Hospital, based on the clinical and electrophysiological findings. Their mean age of the patients was 56.5 years (range 36-66). They fulfilled the following features ; 1) chronic progressive muscular weakness with or without bulbar/pseudobulbar palsy (PBP), 2) upper motor neuron involvement signs, 3) little or no sensory or autonomic disturbances, 4) chronic neurogenic changes in the electromyographic findings and 5) no other specific causes. We selected the cases in whom we determined the SEPs in both the upper and lower limbs. There were no familial cases. We also excluded any cases with spinal progressive muscular atrophy, bulbospinal muscular atrophy and multidfocal motor neuropathy because of the absence of upper motor neuron signs. Twelve patients were classified as having typical ALS, upper motor neuron dominant type ALS, and ALS with a bulbar onset. Typical ALS was defined as progressive paralysis with both upper (increase in tendon reflexes and/or pathological reflexes) and lower (muscular atrophy and/or fasciculation) motor neuron signs. Upper motor neuron dominant type was defined as a subtype with an onset of upper motor neuron disturbances including PBP and little or no lower motor neuron signs. ALS with a bulbar onset was defined as that showing bulbar weakness with upper and lower motor neuron signs. No sensory disturbance was seen in any patients thus implying the dysfunction of the long fiber tracts of the spinal cord. Cervical MRIs of sagittal T2-weighted image (TE 3,000 ms, TR 90 ms) were evaluated to check for cervical spinal stenosis according to the grading system modified from that of Muhle et al.[10], which is described in Table 1. A plain X-ray of the neck was also used to evaluate the minimal antero-posterior diameter.

2.2. Electrophysiological studies

Median and posterior tibial nerve SEPs were recorded as previously described[5)15)]. In brief, electrical stimulation was given to the median nerve at the wrist at a rate of 5 Hz. The peak latencies of the negative wave at Erb's point (N9), the negative wave recorded over the 7th cervical spine (N13) and the negative wave of the contralateral parieral scalp (N20) were all measured. The interpeak latencies (IPL) between N13 and N20 were measured as a central sensory conduction time (CSCT). The IPL of N9-N13 was also measured. The posterior tibial nerve was stimulated at the ankle at a rate of 2 Hz. The peak latencies of the negative wave at 12th thoracic spinous process (N20) and the positive wave over the vertex (P37) were measured. The IPL between N20 and P37 were also measured as CSCT for lower limbs. The responses was bandpass filtered between 5 and 1,500 Hz. The visual evoked potentials (VEPs) to a black-white checkerboard pattern reversal at a rate of 1 Hz were recorded and the peak latency of the major positive wave (P100) was also measured. The bandpass of the recording system was 0.5-120 Hz. The brainstem auditory evoked potentials (BAEPs) were recorded from the vertex. The latencies of waves I, III and V and the IPLs of I-III, III-V and I-V were measured. The bandpass of the recording system was 5-1,500 Hz. Motor evoked potentials (MEPs) were recorded from the abductor pollicis brevis and abductor hallucis muscles as previously described (Tobimatsu-Sun). The hand motor area and

Table 1 Clinical, radiological and electrophysiological findings in the patients.

			Clinical findings			Radiological findings			EMG findings		SEP findings				MEP findings			
						plain X-ray	MRI				Median nerve		Tibial nerve		U/E		L/E	
No.	Age	Sex	Clinical type	neck pain	Sensory disturbance	mAPD	Cervical spondylosis	Cord compression	Sural SCV (m/s)	Needle EMG	R	L	R	L	R	L	R	L
1	54	F	PBP	(−)	(−)	14	(+)	(+)	45	(++)	N13-N20↑	N	N20-P37↑	N	A	A	A	A
2	60	M	PBP	(−)	(−)	15	(+)	(±)	37 (Median n)	(+)	N9↑	N9↑	N20-P37↑	N20-P37↑	A	A	A	A
3	57	F	PBP	(−)	rt. L/E mild hypesthesia	15	(+)	(−)	NE	(±)	N	N	N20-P37↑	N20-P37↑	A	N	A	A
4	64	F	ALS+bulbar	(+)	(−)	8	(+)	(+)	NE	(+)	N	N	N	N	N	A	N	N
5	65	F	ALS+bulbar	(−)	(−)	13	NE	NE	37	(++)	N	N	N	N	N	N	N	N
6	46	M	ALS	(+)	(−)	15	(+)	(−)	NE	(++)	N	N	N	N	N	A	A	A
7	64	F	ALS	(+)	(−)	12	(+)	(−)	37	(++)	N	N	N	N	A	A	A	A
8	66	M	ALS	(+)	(−)	15	NE	NE	37	(++)	N	N	N	N	N	N	N	A
9	54	F	ALS	(+)	lt. L/E paresthesia	11	(+)	(−)	35	(±)	N	N	N	N	A	A	A	A
10	62	F	ALS	(+)	(−)	13	(+)	(−)	42	(++)	N	N	N	N	NE	NE	A	N
11	51	M	ALS	(+)	(−)	14	(+)	(+)	35	(++)	N	N	N	N	N	N	A	A
12	36	M	ALS	(+)	(−)	11	(+)	(+)	34	(++)	N	N	N	N	N	NE	A	A

Age means the age on the examination at our hospital.

Abbrebviations: M=male; F=female; PBP=progressive bulbar palsy; ALS=amyotrophic lateral sclerosis; ALS+bulbar=ALS with bulbar onset; R=right; L=left; U/E=upper extremities; L/E=lower extremities; mAPD=minimal antero-posterior diameter; NE=not examined; SCV=sensory conduction velocity; EMG=electromyography; N=normal; A=abnormal; SEPs=somatosensory evoked potentials; MEPs=motor evoked potentials

Cord compression on MRI (T2-weighted image)

− : no or partial obliteration of the anterior and/or posterior subarachnoid space

± : complete obliteration of the anterior and/or posterior subarachnoid space

+ : anterior and/or posterior cord compression

Needle EMG

± : neurogenic changes in one muscle

+ : neurogenic changes in two muscles

++ : neurogenic changes in three or more muscles

cervical roots were stimulated by an eight-shaped magnetic coil to obtain hand MEPs. The leg motor area and lumbar roots were also stimulated by the magnetic coil to determine the leg MEPs. The central motor conduction time (CMCT) was determined by subtracting the onset latency of the cervical (or lumbar) MEPs from that of the cortical MEPs. The filter was set at between 50 Hz and 3,000 Hz.

The sensory nerve conduction velocties of sural or median nerve were measured. Needle electromyography (EMG) was also performed to assess the degree and extent of denervation.

3. Case reports

3.1. Case 1

A 53-year-old woman, who had had schizophrenia at 29 years of age, insidiously developed weakness in her right upper and lower limbs. Soon thereafter, she began to experience dysarthria and the symptoms progressed gradually. At the age of 54, she was admitted to our department. She had a brother with schizophrenia but no family history of motor neuron disease. A neurological examination revealed her to be mentally alert while she showed a mildly impaired WAIS-R score (IQ 65). She had dysarthria and mild sensorineural hearing loss in her right ear. There was muscular weakness in all four limbs with right dominance but neither muscular atrophy nor fasciculation was found. Her muscle tone generally increased, while her tendon reflexes were increased in all four limbs and Babinski's sign was positive bilaterally. Her jaw jerk also increased. Her gait was mildly spastic. In addition, she showed a slightly impaired position sense only in her right upper limb.

3.2. Case 2

A 60-year-old man developed dysarthria, followed by muscular weakness in his right upper and lower limbs six months later. One year after onset, he was admitted to our department. A neurological examination revealed mild facial muscular weakness and severe dysarthria. He had mild muscular weakness on his right side and mild atrophy in all limbs, but on fasciculations were apparent in either his tongue or limb muscles. The muscle tone was normal. The tendon reflexes were exaggerated in all limbs and jaw jerk was hyperactive. Babinski's sign was positive bilaterally. There was no sensory disturbance.

3.3. Case 3

A 55-year-old woman noticed progressive dysarthria. A few months later, she developed progressive weakness in her right lower limb, which was followed by weakness in her right upper limb. Her symptoms progressed gradually and finally she was admitted to our hospital two years after the onset. An neurological examination showed dysphagia, slurred speech and mild limb muscle weakness on her right side. Neither muscular atrophy nor fasciculation including bulbar muscle was found. The muscle tone was mildly spastic on the right side. The tendon reflexes increased in her upper limbs, especially on the right side and Babinski's sign was positive on the right. Jaw jerk also increased. She had mild hypesthesia in her right L5/S1 segment. Otherwise her neurological status was normal.

4. Results

Table 1 summarizes the clinical, radiological and electrophysiological findings of the patients. Of the 12 patients, 3 had an upper motor neuron dominant type ALS (cases 1-3), 2 had ALS with bulbar onset (cases 4, 5) and 7 had typical ALS (cases 6-12). These 3 patients

(cases 1-3) were also characterized according to their degree of pseudobulbar palsy (PBP). SEP abnormalities were only present in these 3 cases. All 3 had a prolonged N20-P37 in the tibial nerve SEPs. Case 1 had a unilateral prolongation, while the others had a bilateral prolongation. In case 1, the prolonged N13-N20 with normal N9 and N9-N13 interval in median nerve SEPs was observed on the same side of the abnormal tibial nerve SEPs (Fig. 1). Case 2 had bilateral prolonged N9-N13 and N13-N20, while patient 3 showed normal median nerve SEPs. In case 3, mild hypesthesia was observed in her right L5/S1 region despite normal N20 of tibial nerve SEPs without laterality of the N20-P37 interval.

The MEPs were abnormal in all 3 PBP patients. The prolonged CMCT was the most common finding. However, in case 2, the CMCT of right upper limb and that of the left lower limb were within the normal limits. Moreover, the patient had bilateral prolonged MEP latency elicited by lumbar root stimulation. In case 3, the CMCT of left upper limb was within the normal limits. Eight of the other 9 patients also showed abnormal MEPs at least in one limb. We also examined BAEPs in case 1 and VEPs in these 3 patients. Case 1 had prolonged I-III interval by right ear stimulation. VEPs were normal in all cases.

We measured sural nerve conduction velocity in 8 patients including case 1 but no abnormalities were found. The sural nerve conduction velocity in case 2 was not examined, however, the sensory conduction velocity, of median nerve was mildly prolonged bilaterally. Needle EMG showed neurogenic changes in the fasciculation potentials, giant potentials and polyphasic potentials with a long duration in more than 3 muscles in 8 patients (cases 1, 6-12). However, 2 patients with PBP (cases 2, 3) and 2 with ALS with a bulbar onset had neurogenic changes only in one or 2 muscles with distal dominance.

Radiologically, cervical MRI showed CS in 2 of 3 PBP and in 7 of the other 9 patients (Table 1). Case 1 had right predominant cervical cord compression without any sensory disturbances, according to the side of SEP abnormalities. Similarly, 3 of the 7 patients with cervical spondylosis (CS) had cervical cord compression.

5. Discussion

In this study, 3 ALS patients had SEP abnormalities, which were all upper motor neuron dominant type ALS presenting with PBP cliniacally. These 3 patients were characterized by the presence of both an upper motor neuron sign (hyperreflexia and positive Babinski's sign) and PBP, showing dysarthria from the early stage of the illness. In contrast, they showed little sign of lower motor involvement (muscular atrophy and fasciculation, hyporeflexia). EMG findings also indicated less involvement of lower motor neuron.

Electrophysiologically, these 3 patients had a prolongation of CSCT of tibial nerve SEPs. In addition, case 1 had prolonged N13-N20 in median nerve SEPs on the side of abnormal tibial nerve SEPs, which probably reflects the subclinical involvement of the posterior column. Case 2 had bilateral prolonged N9 in median nerve SEPs. We cannot say for certain why N9 was bilaterally prolonged, however, this is not likely due to polyneuropathy because N20 in the tibial nerve is within the normal limits bilaterally. The delayed N9 may therefore be indicative of the involvement of spinal ganglia in ALS[6]. Our findings thus confirm those of previous reports[1)3)12)], which show that abnormalities can occur outside the motor system in sporadic ALS. However, CS was observed in 2

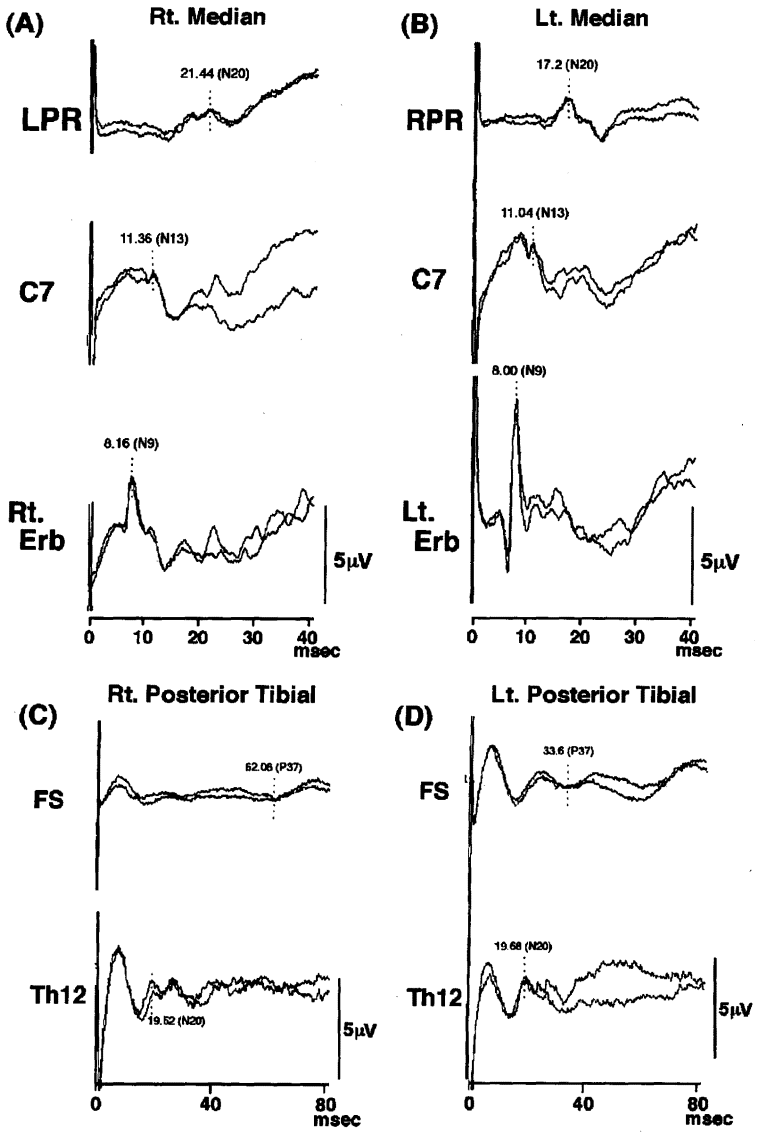

Fig. 1 SEP findings in case 1. Right median nerve SEPs showed abnormal N13-N20 with normal N9-N13 (A) while those on the left side were normal (B). Right posterior tibial nerve SEPs revealed a prolongation of N20-P37 with normal N20 (C) while those on the left side were normal (D).
Abbreviations: Erb=Erb's point; LPR=Left post-Rolandic area; RPR=Right post-Rolandic area; FS=Foot sensory area (2cm posterior to Cz); C7=Spinous process of the 7th cervical vertebra; Thl2=Spious process of the 12th thoracic vertebra

of 3 PBP patients and one had cervical cord compression. One may thus argue that the SEP abnormalities in these patients resulted from CS, because patients with cervical spondylotic myelopathy often show SEP abnormalities[7)9)11)17)18)20)]. Common median nerve SEP abnormalities in CS include the prolonged N9-N13, absent or reduced N13 and prolonged CSCT. In addition, the prolonged N20-P37 of tibial nerve SEPs also suggest the presence of cervical myelopathy. However, it seems reasonable to suppose that the SEP abnormalities in our patients resulted from ALS itself for the following reasons. Firstly, Masur et al.[7)] reported that the prolonged CSCT of tibial nerve SEPs occurred frequently in patients with segmental sensorimotor symptoms of the upper limbs. However, our patients showed no deep sensory impairment with segmental signs thus implying cervical myelopathy. Moreover, the findings that bilateral prolonged N9 of median nerve SEPs in case 2 and normal N9-N13 with prolonged CSCT in all the three patients are contradictory to cervical spondylotic myelopathy[14)]. Secondly, 3 of 7 ALS patients had CS with cervical cord compression but they did not show any abnormal SEPs. Thirdly, case 1 had abnormal BAEPs, thus suggesting the involvement of the auditory pathways in the brainstem. These findings correlated with those from a previous report[8)] in which BAEP abnormalities tended to occur in patients with abnormal SEPs. It is therefore likely that the abnormal median and tibial nerve SEPs in our patient result from the degenerative process of ALS itself but not from cervical spondylotic myelopathy.

Previous reports revealed that from 14～34% in upper limbs and from 30～59% in the lower limbs of ALS patients showed abnormal SEPs[2)8)14)]. However, previous reports did not describe any clinical characteristics of such patients. Hudson[3)] found the incidence of posterior column involvement to be less than 10% in sporadic ALS by autopsy. In previous reports[1)12)], ALS patients with posterior column involvement revealed by autopsy were limb onset ALS. The clinical pictures of our patients were not consistent with these reports. However, from the above mentioned observations, upper motor neuron dominant type ALS patients, especially those associated with PBP may tend to show SEP abnormalities and other multimodal abnormalities, thus suggesting that such patients may form a distinct clincal subtype of ALS. In the future, however, this hypothesis must be further proved based on the pathological findings of a larger number of patients.

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(和文抄録)

体性感覚誘発電位異常を呈した弧発性筋萎縮性側索硬化症の3症例

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目的：筋萎縮性側索硬化症（ALS）における感覚系の障害の報告は散見されるが，そのような症例の臨床的特徴はあまり知られていない．今回，我々は体性感覚誘発電位（SEP）で異常を呈した3例を経験したので，臨床的，電気生理学的特徴を報告する．方法：今回の3例を含め上下肢のSEPを測定した12例の弧発性ALS症例（検査時33-66歳）について臨床像，針筋電図，感覚神経伝導速度，運動誘発電位（MEP），頚部MRIまたは単純X線写真を評価した．結果：3症例では臨床的に仮性球麻痺を含む上位運動ニューロン障害優位の特徴を認めた．全例後脛骨神経刺激SEPの異常を認め，うち2例では正中神経刺激でも異常を示した．3症例はMEPでも中枢伝導時間を中心とした異常を認め，1例は一側性の聴性脳幹反応の異常があった．筋電図では下位運動ニューロンの障害は比較的少ないことが示された．結論：仮性球麻痺を伴う上位運動ニューロン障害が優位な弧発性ALSでSEP異常を伴う症例は，臨床的にALSの亜型である可能性が示唆された．