

[ CASE REPORT ]

## Status Cataplecticus with Rapid Eye Movement Sleep Excess in Late-onset Narcolepsy Type 1

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### Abstract:

A 57-year-old man presented with difficulty speaking and walking along with increased daytime somnolence. His symptoms fluctuated throughout the day but never completely disappeared. A neurological examination revealed mild dysarthria, limb weakness, and staggering gait. Polysomnography showed rapid eye movement (REM) sleep excess (55.0%). Multiple sleep latency tests revealed a mean sleep latency of zero minutes with sleep-onset REM periods in all naps. The Orexin-A concentration in the cerebrospinal fluid was low (50.8 pg/mL). Human leukocyte antigen testing demonstrated DQB1\*0602 positivity. His neurological symptoms were relieved by clomipramine. Thus, he was diagnosed with late-onset narcolepsy type 1 with status cataplecticus.

**Key words:** narcolepsy, cataplexy, sleep latency, REM sleep, status cataplecticus

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### Introduction

Narcolepsy type 1 is a rare hypersomnolence disorder characterized by the presence of cataplexy and orexin deficiency in the hypothalamus (1, 2). Cataplexy is a specific symptom of narcolepsy and refers to transient episodes of muscle weakness triggered by emotions (2). The duration of cataplectic attacks is usually less than two minutes (3).

The peak onset of narcolepsy is around the second to third decade of life, with few patients developing the disease after the fifth decade (4, 5). An onset at a young age is associated with increased severity of the disease, while late-onset cases show relatively mild excessive daytime sleepiness (EDS) and cataplexy (5).

We herein report a case of late-onset narcolepsy type 1 presenting with persistent neurological symptoms.

### Case Report

A 57-year-old man presented to the neurological department with difficulty speaking and walking. He had no medical or family history of neurological or sleep disorders. His

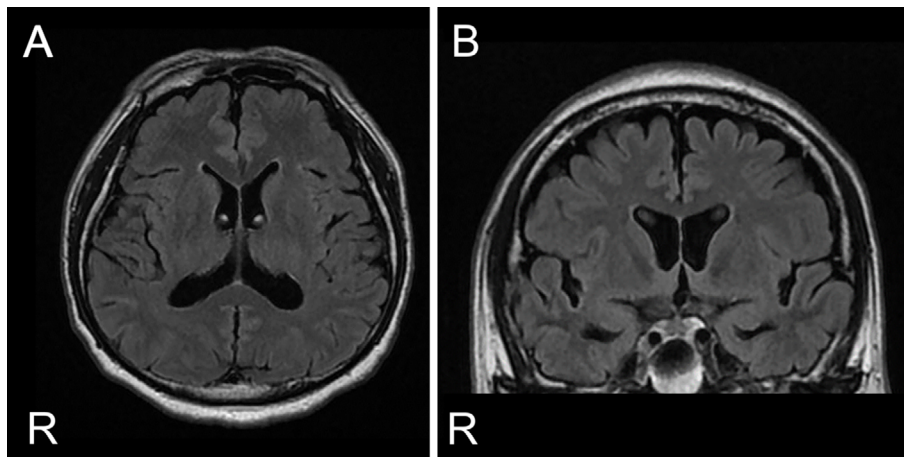
body mass index was 19.8. The patient experienced weakness in his limbs, and difficulty walking emerged one month before presentation. Since then, he had been feeling constantly unsteady when walking. Simultaneously, he noticed increased daytime somnolence and excessive dreaming, despite having more than seven hours of sleep at night. He became sleepy right after he woke up in the morning and began to fall asleep during work. He also developed difficulty speaking two weeks before presentation. His speech and gait disturbances were persistent; they fluctuated throughout the day but never completely disappeared. There was no correlation between the intensity of his sleepiness and the degree of his speech and gait disturbances. He had never experienced such weakness or daytime drowsiness in the past. He took naps when he experienced severe weakness in his limbs. However, the weakness was not relieved by napping. There were no specific triggers or situations, including sudden emotions, that caused worsening of the symptoms. He had experienced sleep paralysis once at 20 years old, but it had not happened again. Hypnagogic hallucination was not noted.

A neurological examination revealed mild dysarthria, symmetrical proximal muscle weakness in the limbs (shoul-

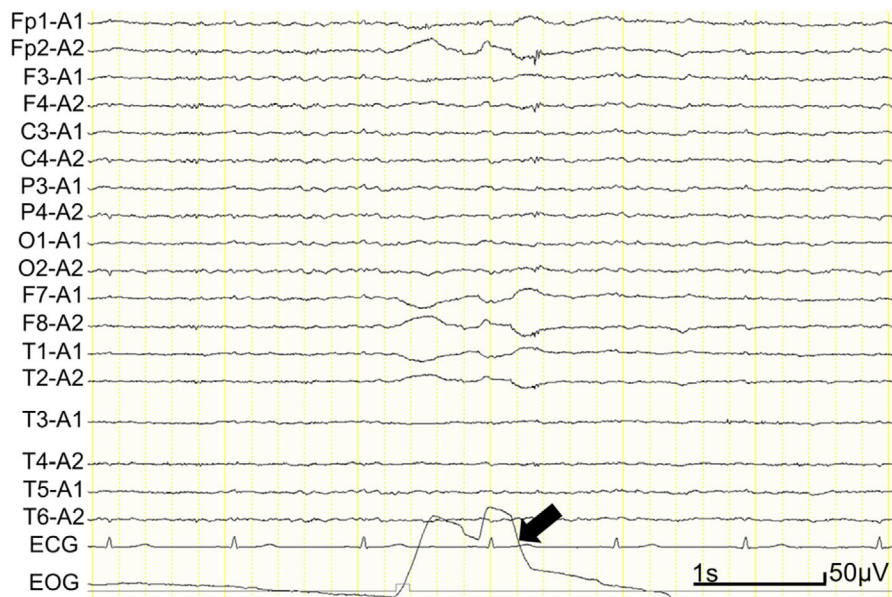
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**Figure 1.** Brain magnetic resonance imaging of the patient. Axial (A) and coronal (B) fluid-attenuated inversion recovery images show no abnormalities in the brain parenchyma including the hypothalamus.



**Figure 2.** Short-term electroencephalography of the patient. Electroencephalography shows a low-amplitude, mixed-frequency background soon after the beginning of the test. Brisk eye movements are also observed (arrow). ECG: electrocardiogram, EOG: electrooculogram

der abduction and hip flexion were grade 4 on the Medical Research Council scale), and staggering gait. The facial and neck muscles of the patient were preserved. His biceps tendon reflex was weak, while his triceps tendon reflex and patellar tendon reflex were normal. His sensory function and motor coordination of limbs were normal, and the extensor plantar reflex gave a flexor response. Brain magnetic resonance imaging (MRI) was unremarkable (Fig. 1). Short-term electroencephalography (EEG) showed no epileptic discharge. However, immediately after the test, there was poor alpha activity and a low-amplitude, mixed-frequency background with brisk eye movements (Fig. 2). A laboratory examination revealed a normal creatine kinase level, thyroid function, and C-reactive protein level. Test results for

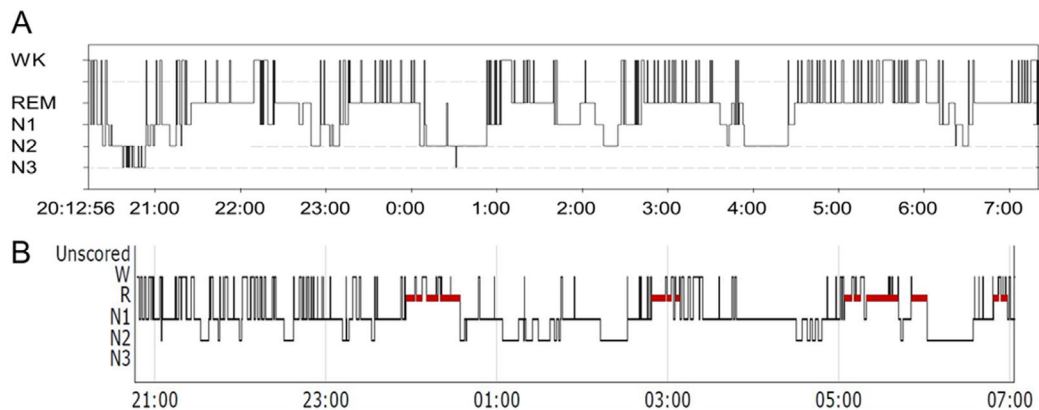
autoantibodies, including anti-acetylcholine receptor antibody and anti-aquaporin-4 antibody, were negative. A cerebrospinal fluid (CSF) analysis revealed elevated protein (65 mg/dL) but a normal cell count and glucose levels. The immunoglobulin G index was normal, and the oligoclonal band was negative. These results did not reveal the cause of his neurological symptoms, but as he also complained of EDS, additional tests were performed.

His score on the Japanese version of the Epworth Sleepiness Scale (JESS) was 18/24 (6). Polysomnography (PSG) showed that among the sleep stages, rapid eye movement (REM) sleep was predominant (55.0%), and moderate obstructive sleep apnea (OSA) (apnea-hypopnea index, 24.4/h) without periodic limb movements was revealed (Table 1,

**Table 1. The Patient's Polysomnography-based Sleep Parameters.**

Sleep period time (SPT), min	666.0	Sleep efficiency, %	84.6
Total sleep time (TST), min	563.5	Apnea index (AI), /h	4.3
%Sleep stage		Obstructive sleep apnea index, /h	4.0
Stage W, % (%SPT)	15.4	Central sleep apnea index, /h	0.0
Stage N1, % (%TST)	20.5	Mixed sleep apnea index, /h	0.3
Stage N2, % (%TST)	22.6	Hypopnea index, /h	20.1
Stage N3, % (%TST)	1.9	Apnea hypopnea index (AHI), /h	24.4
Stage R, % (%TST)	55.0	Lowest sleep SpO <sub>2</sub> , %	89
Wake after sleep onset (WASO), min	102.5	3% oxygen desaturation index (ODI3%), /h	8.8
Arousal index, /h	25.3	Periodic limb movement (PLM) index, /h	0.0

The recording was scored by the American Academy of Sleep Medicine scoring manual version 2.5.



**Figure 3.** Chronological hypnogram of the patient. (A) On polysomnography (PSG) performed before treatment, stage R accounts for 55.0% of the sleep. Respiratory effort-related arousals were observed mainly during rapid eye movement (REM) sleep periods. (B) On PSG performed after treatment, stage R accounts for 18.3% of the sleep. The recordings were scored by the American Academy of Sleep Medicine scoring manual version 2.5. N1: Stage N1, N2: Stage N2, N3: Stage N3, REM or R: Stage R, WK or W: Stage W

**Table 2. The Results of the Multiple Sleep Latency Test.**

Nap	Start time	Sleep latency, min	Rapid eye movement (REM) latency, minute
1	09:08	0.0	3.0
2	11:01	0.0	2.5
3	13:08	0.0	14.0
4	14:59	0.0	0.0
5	16:59	0.0	1.0
	<b>Mean</b>	0.0	4.1

The recording was scored by the Rechtschaffen and Kales method.

Fig. 3A). REM sleep without atonia was not observed. The multiple sleep latency test (MSLT) revealed a mean sleep latency of zero minutes, indicating that he was already asleep when he was placed in the supine position and the test was started. Furthermore, all five naps showed sleep-onset REM periods (SOREMs) (Table 2). The orexin-A concentration in CSF was low (50.8 pg/mL). Human leukocyte antigen (HLA) testing demonstrated DQB1\*0602 positivity. HLA DRB1 testing was not performed. Based on these clinical

findings, he was suspected of having narcolepsy type 1.

The patient did not want to use continuous positive airway pressure (CPAP) or an oral appliance for moderate OSA; therefore, we only provided guidance on sleep posture. The patient was initially treated with clomipramine and modafinil for narcolepsy type 1. Before the treatment, his dysarthria, muscle weakness in the extremities, and gait disturbance persisted almost all day, but with 50 mg clomipramine daily, these symptoms disappeared. His EDS was

also reduced to a certain degree with 200 mg modafinil daily, and the JESS score improved to 8/24. However, even with the medication, the patient continued to have mild daytime sleepiness; therefore, he was given a combination of modafinil (200 mg daily) and pemoline (25 mg daily). After treatment, his mean sleep latency was 29 minutes and SOREMs were not observed in the maintenance of wakefulness test (MWT). On PSG the night before the MWT, the percentage of REM sleep became normal (18.3%) (Fig. 3B). At the follow-up one year after the onset, his symptoms were stable with medication, and there were no novel neurological symptoms.

## Discussion

The patient was diagnosed with late-onset narcolepsy type 1 based on the current criteria, which include EDS for more than 3 months, a mean sleep latency of <8 minutes with SOREMs on MSLT, and orexin-A deficiency in the CSF (1). Positivity for the HLA DQB1\*0602 genotype is also associated with narcolepsy (2). The patient had moderate OSA, which alone can cause hypersomnia and shorten sleep latency with SOREMs on MSLT (7). However, it cannot explain the orexin-A deficiency in CSF, suggesting that narcolepsy type 1 and OSA coexisted. Although we were unable to confirm the efficacy of CPAP or an oral appliance in this patient, OSA has been reported to play a minor role in the severity of EDS in narcolepsy (8). Thus, his severe EDS was likely due to the late-onset narcolepsy (9).

Another interesting finding was the presence of persistent neurological symptoms such as dysarthria, muscle weakness in the limbs, and gait disturbance. Secondary narcolepsy, which can be complicated by neurological symptoms, includes brain tumors, demyelinating disorders, vascular disorders, and encephalitis (10). However, no other possible causes of secondary narcolepsy were found by MRI, EEG, or laboratory tests. Importantly, the patient's neurological symptoms were relieved by clomipramine, and the improvement was sustained for at least one year. Although we did not perform comprehensive testing for autoantibodies of encephalitis, an improvement in the clinical course without immunosuppressive treatment makes autoimmune encephalitis seem unlikely. Therefore, we suspected that the patient had status cataplecticus caused by late-onset narcolepsy type 1.

Cataplexy refers to transient episodes of muscle weakness associated with narcolepsy, and unusual cataplexy that occurs repeatedly for hours or days is called status cataplecticus (11). The association of status cataplecticus with late-onset narcolepsy has been previously reported, but the duration of symptoms at the onset is usually short, with an intermittent period of no symptoms (12, 13). In contrast, our patient presented with persistent neurological symptoms from the onset, which may be the most severe form of status cataplecticus.

REM sleep excess on the initial PSG was also a characteristic finding in this patient. In previous studies, such a

high increase in REM sleep on a PSG was rare in patients with narcolepsy (14, 15). Several causes have been reported to increase the percentage of REM sleep, such as REM sleep deprivation, depression, undergoing CPAP titration, or withdrawal of REM-suppressing medication, and drugs (16). More recently, increased REM sleep time in a patient with multiple sclerosis has been reported (17). In our patient, there was no apparent cause for the increase in REM sleep. Although the relationship between the increase in REM sleep and status cataplecticus is unclear, it is interesting that both neurological symptoms and PSG findings became normal after the patient was treated with clomipramine. Because REM sleep predominance (27.9%) in a patient with status cataplecticus was also reported previously (12), a further study is needed concerning the relationship between REM sleep and status cataplecticus.

It is challenging for clinicians to diagnose late-onset narcolepsy with status cataplecticus. This is because narcolepsy is rare in older individuals; they have a higher incidence of many other neurological diseases, and standard tests, such as MRI, are unremarkable. Given that a misdiagnosis can worsen the patient's quality of life (13, 18), a precise diagnosis of late-onset narcolepsy is important. The key to the diagnosis is to recognize the presence of EDS and to perform sleep-related tests as demonstrated in our report. A detailed medical history may improve the diagnostic accuracy of this unusual late-onset narcolepsy.

In conclusion, we report a case of late-onset narcolepsy type 1 presenting with dysarthria and gait disturbance due to status cataplecticus. Status cataplecticus may cause persistent neurological symptoms from the disease onset, and the diagnosis of this condition is challenging for clinicians. REM sleep excess on the PSG was also a characteristic finding in the patient, and a further study is needed to clarify the relationship between REM sleep and status cataplecticus.

Written informed consent was obtained from the patient.

**The authors state that they have no Conflict of Interest (COI).**

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