



Prolonged Loss of Consciousness in Parkinson's Disease

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Abstract

Background: Loss of consciousness is fairly common in Parkinson's disease, which occurs as syncope associated with postural hypotension based on autonomic dysfunction, or as sleep disorder which consists of excessive daytime sleepiness and sleep attacks.

Case presentation: Ten patients with Parkinson's disease are reported who showed episodes of loss of consciousness lasting for 4-24 h that appeared to be deep sleep or a coma, and could not be roused even by strong painful stimuli. After four hours or more, they spontaneously resumed consciousness without sequelae.

Discussion and conclusion: The diagnostic criteria of these two disorders in ICSD-3 differ from the prolonged loss of consciousness in my cases. As it has brought great concern to family members, medical staff, and emergent hospital personnel, we must pay more attention to this type of loss of consciousness.

Keywords: Unconsciousness; Sleep disorder; Hypersomnia; Parkinson's disease; Postural hypotension

Introduction

Loss of consciousness is common in Parkinson's disease (PD), which can occur as syncope associated with postural hypotension based on autonomic dysfunction [1]. It occurs also as sleep disorder, known as hypersomnia of central origin, mainly consisting of excessive daytime sleepiness (EDS) and sleep attacks [2]. EDS and sleep attacks in PD may be evoked naturally or with drugs, both usually appearing as repeated drowsiness and/or short naps in the daytime [2]. In the International Classification of Sleep Disorders-Third edition (ICSD-3), EDS in PD is classified as "hypersomnia due to a medical disorder", while sleep attacks in PD (usually not associated with cataplexy) are classified as "narcolepsy, type 2" [3].

I experienced ten cases of prolonged loss of consciousness lasting for several hours that is neither EDS nor ordinary sleep attacks. In ICSD-3, persistent loss of consciousness in PD, as seen in my patients, is not precisely described [3]. Epilepsy must be excluded in cases of loss of consciousness in PD, because it can occur in PD more frequently than in the general population, showing an adjusted odds ratio in PD patients of 1.68 compared with PD-free individuals [4]. There were no clinical findings suggestive of epilepsy at the time when this phenomenon appeared in my patients.

Case Presentation

The ten patients with PD showed episodes of loss of consciousness lasting for 4-24 h, which appeared to be deep sleep or a coma and could not be roused even by strong painful stimuli. After four hours or more, they spontaneously resumed consciousness without sequelae. The clinical symptomatology of three representative patients among these ten is described below.

Case 1

A 72-year-old woman was hospitalized for rehabilitation. She had developed PD at 54 years old and been treated with anti-Parkinson drugs, including levodopa-carbidopa, selegiline, and pramipexole. The drugs were effective without causing EDS, although motor disturbances gradually increased in severity to Hoehn-Yahr (H-Y) stage 4. Then, she suffered from marked freezing gait, and motor rehabilitation was initiated after hospitalization. Before lunch, after five days' admission, she was found to be sitting in the wheelchair, unable to be awake and looking deeply asleep or in coma. A neurologic examination revealed no motor responses to painful stimuli. Her vital signs including pulse oximetry data were unremarkable except for unconsciousness. Her blood chemistry examination findings were within normal limits, and electroencephalogram (EEG) showed a sleep pattern of deep grade. She was observed with venous infusion of isotonic solutions, and about 24 h later, she regained consciousness without neurologic sequelae. According to her family, this was the first episode of abnormal loss of consciousness, and throughout the following admission period of a month there occurred no such events.

Case 2

A 76-year-old woman with PD had been cared by her family at home for 10 years after the onset. She had been given levodopa-carbidopa-entacapone compounds and selegiline and was able to walk with a walker (H-Y stage 4) but needed help bathing. She showed postural hypotension, for example, with a blood pressure of 135/78 mmHg in the supine position and 94/50 mmHg in the upright position. She sometimes felt faintness while standing; she soon regained her usual alertness.

One day, while bathing under the care of her family, she suddenly lost consciousness. This time, however, she remained completely

motionless, and her eyes were closed without response to stimuli. She did not look pale, and her blood pressure (examined with a home blood pressure manometer) was 120/74 mmHg with a heart rate of 64/min showing a regular rhythm. As she did not recover consciousness even after 30 minutes, she was emergently brought to the hospital. On arrival she looked like in deep coma, although her vital signs other than consciousness were normal. The laboratory examinations were all within normal limits, including an electrocardiogram (ECG) and head CT, and twelve hours later, she gradually recovered consciousness and was taken home without sequelae. Six months later, she experienced a similar loss of consciousness episode while sitting in a chair and was transferred to the same emergent hospital. This time, she recovered consciousness within seven hours. After these episodes, she experienced loss of consciousness a third time 1 year later and was observed at home, recovering consciousness within 4 h. At home, a 24-hour Holter ECG was examined, showing normal results.

Case 3

A 78-year-old man had been hospitalized for 2 years due to advanced PD. At 63 years old, he developed rest tremor of the left hand, followed by increasing rigidity of all limbs and gait disturbance. Head magnetic resonance imaging (MRI) revealed no specific changes, and he was diagnosed with PD and given levodopa, followed by the addition of selegiline and pramipexole, which were effective in improving his motor symptoms of PD without causing EDS.

At 70 years old he developed wearing-off symptoms and freezing gait. The findings on dopamine transporter scintigraphy using ¹²³I-ioflupane and cardiac scintigraphy using ¹²³I-meta-iodobenzylguanidine were compatible with PD. At 76 years old, the severity of his dementia and dysphagia increased, so he was admitted to our hospital, and percutaneous endoscopic gastrostomy was performed. Thereafter, he was given only levodopa-benserazide compound (300/75 mg/day) as an anti-Parkinson drug. He sometimes experienced aspiration pneumonia. At 77 years old, he was bedridden, only occasionally opening his eyes, making random limb movements.

One day, at about 9 o'clock in the morning, soon after a meal, a nurse found him with his eyes closed, completely motionless. He would not open his eyes or move his limbs even in response to strong painful stimuli. A neurologic examination showed a pupillary size of 1 mm bilaterally with a prompt response to light. He appeared to be in a deep coma. However, his vital signs were normal, including his blood pressure, heart and respiratory rates and pulse oximetry data. Emergent head CT revealed no abnormal radiological changes except for atrophic brain. His serum chemistry including blood glucose concentrations, and CBC were within normal limits, as before. EEG revealed 3 to 5 Hz slow waves in basic activity with a roughly 50 μV amplitude and no epileptic abnormalities. He was kept under observation, and ten hours later, he regained consciousness, again showing eye opening and random limb movements without specific sequelae. No repeated episodes were noted for the next year.

Among the 10 patients with PD who showed episodes of prolonged loss of consciousness, the duration was 4-24 h, although typically they aroused within 5-10 h. In the three patients above described, unconsciousness occurred fairly suddenly followed by a prolonged loss of consciousness. However, among the remaining seven, there were three cases whose initiation of unconsciousness was obscure. The numbers of attacks were one in two patients, two in four patients, three in three patients and four in one patient. During the attacks, the

patients seemed to have fallen into a deep sleep or coma and could not be aroused even by painful stimuli. In all cases, seizure-like motions, such as conjugate deviations of the eyeballs, limb convulsions, and automatism, were not observed. Two patients whose EEG findings were examined while unconscious showed no epileptic patterns. A polysomnographic analysis was not performed in any of the patients. With regard to the severity of PD in these ten patients, the H-Y stage was 3 in one patient, stage 4 in seven patients, and stage 5 in two patients, revealing a tendency to occur more often in patients with advanced stages. Concerning anti-Parkinson drugs, only three patients were taking dopamine agonists at the attacks, revealing that dopamine agonists were not essential for these episodes. Postural hypotension was observed in only two patients, indicating that remarkable autonomic dysfunction was not necessary.

Discussion

According to the ICSD-3, "hypersomnia due to a medical disorder," which includes EDS in PD, occurs every day, persisting for at least three months, and can be evoked by insomnia or anti-Parkinson drugs [3]. And, the sudden onset of sleep, a synonym of sleep attacks in PD, is classified as "narcolepsy, type 2" [3]. In "narcolepsy, type 2" sleep attacks occur every day, persisting for at least three months. When the concentrations of orexin (hypocretin) in cerebrospinal fluid are decreased in patients with sleep attacks, the diagnosis of "narcolepsy, type 1" is appropriate [3].

Regarding EDS in PD, it remains unclear both in ICSD-3 and other reviews [2,5,6]. In addition, another question remains regarding whether or not it may develop into long and deep sleep of up to 24 hours in length, as is seen in the PD patients in this study. And, regarding sleep attacks in PD, they have been usually described as repeated short naps according to the ICSD-3 and other reviews [2,5,6]. The long duration of sleep observed in my PD patients, if the loss of consciousness could be accounted for a sleep disorder, is as long as those of "idiopathic hypersomnia" or "Kline-Levin syndrome" in the ICSD-3. Both of the latter diseases, however, differ essentially from PD in their pathophysiologies. Orexin loss may contribute to sleep disorders in PD patients, particularly by disturbing the sleep/wake regulation machinery and causing hypersomnia episodes [7]. However, the roles of orexin in various types of sleep disorders in PD are unclear at present. Finally, epilepsy may be a possibility. However, there were no such clinical findings as convulsions, automatism and EEG abnormalities, suggestive of epilepsy (Table 1).

	Case 1	Case 2	Case 3
Age	72 year	76 year	78 year
Gender	Female	Female	male
Parkinson's disease onset	54 year	66 year	63 year
anti-Parkinson drugs	levodopa-carbidopa, selegiline, and pramipexole	levodopa-carbidopa-entacapone compounds and selegiline	levodopa, selegiline and pramipexole, levodopa-benserazide compound
Unconsciousness, time span	24 hr	12 hr	10 hr
Other parameters	Hoehn-Yahr (H-Y) stage 4	135/78 mmHg (supine position)	aspiration pneumonia

		94/50 mmHg (upright position)	
		H-Y stage 4	

Table 1: Case presentation of patients affected with Parkinson's disease.

Conclusion

A unique type of prolonged loss of consciousness can occur in PD patients. This is probably a hypersomnia disorder of PD, but it has not been well documented in the ICSD-3 or other reviews. We must pay closer attention to this type of loss of consciousness, as it has brought great concern to family members, medical staff, and emergent hospital personnel.

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Ethics Approval

The Ethics Committee of Tokuyama Medical Association Hospital approved the publication of this article.

Consent for Publication

The family members of the three patients (a daughter of case 1, a daughter of case 2, the wife of case 3) gave informed written consent for publication, respectively.

Authors' Contributions

Mitsunori Morimatsu executed the study and drafted the manuscript.

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