Clinical Corner

Subclinical REM Sleep Behavior Disorder in a Patient With Corticobasal Degeneration

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Summary: Various neurodegenerative diseases have been reported to be associated with rapid eye movement (REM) sleep behavior disorder (RBD). This is the first report of a patient with corticobasal degeneration (CBD) associated with subclinical RBD. A 72-year-old woman was admitted complaining of fine tremor of the right hand and weakness of the right lower extremity. She was diagnosed as having CBD on the basis of clinical features and neuroimaging studies. Her family noticed snoring and increase in sleep talk, but they did not regard them as pathological. All-night polysomnography (PSG) revealed REM sleep without atonia (RWA) during which 14 episodes of talking and singing were observed. They ranged from the utterance of one word to that of comprehensible words of a song for about 3 minutes accompanied by various nonpurposeful movements of the mouth, hands, and limbs. These episodes were not associated with any sleep-disturbed breathing. Future PSG studies on CBD patients together with postmortem analysis of brain stem structures that are crucial for generating REM sleep-related atonia are warranted for further understanding of the pathophysiological mechanism of RBD. Key Words: REM sleep without atonia—REM sleep behavior disorder—Corticobasal degeneration—Polysomnography.

Rapid eye movement (REM) sleep behavior disorder (RBD) is a form of motor dyscontrol characterized by complex, vigorous, frequently violent, and dream-enacting behaviors during REM sleep. In a series of patients documented to have RBD, 48% of them had some central nervous system disorders (1). Among others, neurodegenerative diseases involving brain stem structures as one of the main pathological lesions are often associated with RBD (2–8). Even in a patient with Alzheimer’s disease who presented with RBD, autopsy results showed marked cell loss in the locus coeruleus (9). Recently, we reported REM sleep without atonia (RWA) in patients with early stage olivopontocerebellar atrophy and postulated that RWA might be a subclinical RBD (10). If that is the case, RWA can be regarded as a manifestation of brain stem dysfunction.

Corticobasal degeneration (CBD) is a rare progressive neurodegenerative disease, typical features of which are asymmetric involvement of the cerebral cortex and basal ganglia presenting with focal cortical and parkinsonian symptoms (11–14). Although pathological studies on CBD showed predominant lesions in the cortex and basal ganglia, the midbrain and pontine structures were also reported to be abnormal (11–14). Therefore, it is possible that some sleep abnormality may occur in CBD. To our knowledge, however, sleep abnormality in patients with CBD has not attracted attention. In this paper, therefore, we present clinical and neurophysiological characteristics of subclinical RBD in a patient with CBD.

PATIENT

A 72-year-old woman was admitted in March 1996 because of fine tremor of the right third and fourth fingers and weakness of the right lower extremity that had started 2.5 years earlier. In May 1994 she developed fine tremor of the right hand, for which initial treatment with levodopa/carbidopa (300/30 mg) was ineffective. In March 1995 the dose of levodopa was increased to 500 mg without success. In July 1995 she
started to show dysarthria and loss of volume in her voice. She walked with short steps and little arm swing, and general physical examination upon admission was unremarkable. No mental impairment or mood disturbance was noted, and the Wechsler adult intelligence scale-revised revealed verbal intelligence quotient (IQ) of 111, performance IQ of 75, and full scale IQ of 93. Frontal lobe-released signs such as forced grasp reflex and palmo-mental reflex were positive on the right. The result of Wisconsin card-sorting test was consistent with frontal lobe dysfunction. She showed neither alien limb syndrome nor limb apraxia, but bradykinesia was initially present and markedly asymmetric, much more severe on the right. There was pen-holding dystonic posture in the right hand at rest, and action tremor and cogwheel rigidity in the right arm. Myoclonus was easily evoked in the right arm by tactile stimulation or on action. Cranial nerves were normal. No muscle weakness was revealed in the extremities, and deep tendon reflexes were increased, especially biceps reflex on the right. Coordination of limbs was intact. Brain computerized tomography and magnetic resonance imaging showed mild diffuse atrophy, which was within normal limits for age. N-isopropyl-p-[123I] iodoamphetamine single photon emission computed tomography (SPECT) showed markedly decreased perfusion in the left fronto-temporal regions.

She was fully ambulatory and independent in the activity of daily living at the time of investigation. She had no excessive daytime sleepiness, and sleep apnea had never been witnessed. Her family had noticed snoring and increase in sleep talking in the last few years, but did not regard them as pathological. She had no history of seizure disorder, depression, head injury, or alcohol or other drug abuse. Informed consent was obtained after full explanation about the investigation.

METHODS

All-night polysomnographic (PSG) recordings were performed using the standard technique (15). Electroencephalogram (EEG), electrocuglogram, surface electromyogram (EMG) from submental and tibialis anterior muscles, electrocardiogram, nasal and oral air flow, abdominal movement, and snoring were recorded on a polygraph at a paper speed of 10 mm/second. Oxygen saturation was simultaneously monitored by pulse oxymetry, and the data were transferred for subsequent computer analysis. The patient was continuously and closely monitored with the aid of videotape throughout the recording, and the ongoing behavior and vocalization were charted. Videotapes were reviewed afterwards by making reference to the PSG records.

### TABLE 1. Sleep parameters calculated from the polysomnographic record

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total sleep time (minutes)</td>
<td>308.6</td>
</tr>
<tr>
<td>Sleep efficiency (%)</td>
<td>58.2</td>
</tr>
<tr>
<td>Sleep latency (minutes)</td>
<td>9.0</td>
</tr>
<tr>
<td>WASO (minutes)</td>
<td>180.0</td>
</tr>
<tr>
<td>% Stage 1</td>
<td>7.8</td>
</tr>
<tr>
<td>% Stage 2</td>
<td>56.2</td>
</tr>
<tr>
<td>% Stage 3</td>
<td>16.2</td>
</tr>
<tr>
<td>% Stage 4</td>
<td>0.5</td>
</tr>
<tr>
<td>% Stage REM</td>
<td>0.0</td>
</tr>
<tr>
<td>% Stage RWA</td>
<td>19.3</td>
</tr>
<tr>
<td>No. of REM epochs</td>
<td>1</td>
</tr>
<tr>
<td>REM latency (minutes)</td>
<td>399.5</td>
</tr>
</tbody>
</table>

WASO, wake after sleep onset; REM, rapid eye movement; RWA, REM sleep without atonia.

Staging of wake and non-REM (NREM) sleep was performed according to the criteria of Rechtschaffen and Kales (15), and the modified version by Lapiere and Montplaisir (16) was used for staging REM sleep and RWA. The onset of the first rapid eye movement was taken as the start of a REM sleep period, and the termination of a REM/RWA sleep period was defined by either the occurrence of specific EEG features (K-complexes, sleep spindles, or EEG signs of arousal) or the absence of rapid eye movements during nine consecutive 30-second epochs. RWA was scored either when tonic EMG activity in the chin was present for 50% or more of a 30-second epoch or when the ratio of 3-second mini-epochs containing at least one phasic EMG event within the 30-second epoch was 50% or more. Phasic EMG events were also defined according to Lapiere and Montplaisir (16).

Sleep apnea was defined as cessation of oral and nasal air flow during sleep, and hypopnea as more than 50% reduction in amplitude of air flow, both lasting 10 seconds or longer. Sleep-related oxygen desaturation was determined by decreases in SaO2 by more than 4% from the overnight baseline SaO2 (17). Periodic leg movements during sleep (PLMS) were determined following the Atlas Rules by the Atlas Task Force (18).

RESULTS

Sleep parameters are summarized in Table 1. Although sleep latency was relatively short, the sleep was interrupted for micturition. After this awakening, the patient was awake for about 2.5 hours before initiating sleep again. As a result, only one REM period of 59.5 minute duration was seen in the early morning, and this REM period was staged as RWA. During this period, 14 episodes of sleep talking and singing associated with various movements such as chewing, raising the arm toward the face, waving the hand, and bending the knee were observed. None of these movements
Corticobasal degeneration and REM sleep

C3-A2  F3-C3  C3-P3  P3-O1  F4-C4  C4-P4  P4-O2  LOC-A2  ROC-A1  LOC-ROC  chin EMG  ECG  snore  N/O airflow  abd. mov.  L/TA  R/TA

FIG. 1. Rapid eye movement (REM) sleep without atonia (RWA) seen in the present patient with corticobasal degeneration. There are dense rapid eye movements, and there is phasic electromyogram increase in the chin muscle. The patient was singing during this part of the recording. LOC, left outer canthus; ROC, right outer canthus; N/O, nasal/oral; abd. mov., abdominal movement; TA, tibialis anterior.

appeared to be purposeful, elaborated, or violent. The posture of the patient was basically maintained supine, and no gross body movements were seen during the REM episode. The duration of each episode was from 5 to 180 seconds. The sleep talk was mostly composed of the utterance of one word or one phrase that was easily comprehended, such as “Hai, hai” (Yes, yes), “Sorekara?” (And then?), and “Yokatta-ne” (That was good), and there was one episode of sleep singing that continued for about 3 minutes. When the patient was questioned the following morning, she could not remember engaging in sleep talking and singing. Figure 1 shows the RWA observed in this patient, showing continuously augmented EMG activity in the chin muscle.

Characteristic EEG components of NREM sleep such as vertex sharp waves, sleep spindles, K-complexes, and high-amplitude slow activity were all seen in the record, and there was no difficulty distinguishing NREM from REM sleep. No asymmetry of sleep spindles was observed. Snoring associated with every respiration was detected both by snore sensors and video monitoring, but no apneic or hypopneic events occurred, and no significant oxygen desaturation was noted during NREM sleep. Breathing patterns were very irregular during the REM period, but were not associated with any significant oxygen desaturation. No PLMS was observed.

DISCUSSION

CBD is a clinically and pathologically distinctive neurodegenerative disease. Clinical features include akinesia, dystonia, postural action tremor, reflex myoclonus, hyperreflexia, and cerebral cortical signs, which are all asymmetric at least in the early stage of the illness (11–14), although CBD may have more enlarged clinical spectrum (19). All these signs were seen in the present patient, and indeed asymmetric akinetic-rigid syndrome, limb dystonia, and myoclonus were suggested to be the best predictors for the diagnosis of CBD by one study (20). SPECT findings of markedly asymmetric hypoperfusion supported the clinical diagnosis (21), although we did not have pathological confirmation.

This is the first case of CBD that was extensively studied by using all-night PSG, which revealed various kinds of movements, including talking and singing, exclusively during RWA. RBD is characterized by the appearance of violent, sometimes injurious, and elaborate motor activity during abnormal REM sleep with no proper chin muscle atonia, or RWA. The RWA fea-
ture of this patient is identical to that seen in full-blown RBD, although the motor events during RWA were not violent or injurious.

Pathophysiological explanation of RWA has been based on experimental studies of cats, which showed “oneiric” behaviors following discrete lesions in the dorsolateral rostral pons, in the region of locus coeruleus (22,23). Later, smaller peri-locus coeruleus lesions resulted in RWA without any behavioral manifestations, whereas larger lesions were necessary to produce active behaviors (24). The results of the experimental cat model suggested that manifestation of either full-blown RBD or subclinical RBD was dependent on the specific site of lesion and its extent. These previous experimental findings and the characteristic clinical and PSG features of the present case lead us to conclude that the patient had subclinical RBD.

Although CBD has been regarded as a progressive degenerative disease affecting both cortical and subcortical structures such as thalamus, lentiform nucleus, subthalamic nucleus, red nucleus, and substantia nigra, some autopsy reports have shown prominent cell loss and gliosis also in various nuclei in the brain stem (midbrain tegmentum, locus coeruleus, and raphe nuclei). It is therefore reasonable to assume that crucial structures in the brain stem that are responsible for generating REM sleep-related atonia may be affected in CBD. At the moment, postmortem studies specifically aiming at the brain stem lesions considered to be involved in REM atonia are lacking. More systematic sleep studies on CBD patients and comprehensive postmortem evaluations may result in further knowledge about the pathophysiological mechanism of RBD in CBD.

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