



Case 11. Two Faces of the Medallion

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History

A 76-year-old retired, highly-educated industrialist man with coronary heart disease, diabetes mellitus type 2, silent cerebral ischemia and depression was accepted to our out-patient sleep center with his family in February 2019 with the complaint of abnormal nocturnal behaviors. The family informed that the patient was shouting loudly, behaving as if quarreling with someone, while he was sleeping within that fortnight. The patient reported that he was having dreams involving drowning in the sea, fighting for his life, along with trying to escape from a flood. They told that he might have fallen out of bed in one of these episodes, due to finding him on the floor near his bed. Six months before, a neurologist prescribed an acetylcholinesterase inhibitor (AEI), rivastigmine patch 10 cm² for his forgetfulness and irritability, which he refused to use until recently. At presentation, he could still do shopping with the help of a list, and play cards/backgammon with his cronies. Two months before our encounter, his family observed that he had had some behavior changes, such as becoming more affectionate, more generous and extravagant. Due to this behavior change, he had been persuaded to use rivastigmine transdermal patch 10 cm² regularly. He had been using it for the past 3–4 weeks before presentation.

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He had been on escitalopram 10 mg/day since 2016. Other than snoring and leg movements during sleep, he had no other sleep complaints nor daytime sleepiness. Additionally, he did not have any visual or auditory hallucinations nor delusions. There was no past history of parasomnia.

Examination

Other than absence of Achilles reflexes, neurological examination (including extra-pyramidal system) was normal. Mini-mental state examination was 24 out of 30: the only decline was in orientation (6/10) and recognition (1/3). Body mass index (BMI) was 23 kg/m², neck circumference was 39 cm and Friedman tongue position was IIa.

Investigations/Studies

LDL-cholesterol—143 mg/dL—, fasting blood glucose, kidney, hepatic and thyroid function tests, electrolytes, vitamin B12, folic acid, ferritin and complete blood count were within normal limits. Cranial magnetic resonance imaging (MRI) showed minimal cerebellar atrophy with non-specific T2A hyperintense lesions. A full-night polysomnography with 24 channel EEG was performed while the patient was on rivastigmine. It was concordant with obstructive sleep apnea (OSA) and periodic limb movements of sleep (PLMS) (Table 11.1). He had 8 REM sleep periods with a duration ranging from 1 to 17 min (Fig. 11.1a). In 5 of them, he had REM sleep behavior disorder (RBD) episodes ranging in duration from 20 to 105 s. RBD episodes consisted of meaningless shouting, whispering and gesticulating movements (as if he was pushing something, trying to put something to his mouth, trying to catch or take something with his fingers) (see Video 11.1). REM sleep without atonia (RSWA) was observed throughout REM sleep (Fig. 11.1b, c). There was also an extraordinarily high PLM index of 151/h.

Table 11.1 A full-night polysomnography with 24 channel EEG parameters of the patient

Parameters	Results
Time in bed	390.6 min
Total sleep time	280 min
Sleep period time	340.9 min
NREM Sleep latency	0 min
REM sleep latency	14 min
Sleep continuity index (%)	82.4
Sleep efficiency index (%)	71.9
N1 (%)	60.9
N2 (%)	26.4
N3 (%)	0
R (%)	12.7
Apnea hypopnea index	51.7/h
Respiratory disturbance index	52.1/h
Minimum oxygen saturation	83%
Average oxygen saturation	94%
Total arousal index	37.8/h
Respiratory arousal index	8.6/h
Leg movement arousal index	25.3/h
Spontaneous arousal index	3.9/h
Number of periodic limb movements	706
Periodic limb movement of sleep index	151.3/h
Epileptic activity in EEG	None

The results of the detailed neuropsychological tests which were applied in neuropsychology laboratory showed impairment primarily in memory function along with partial impairment in executive and with no impairment in visual-spatial functions. In the “forgetfulness and behavioral disorders clinic”, he was diagnosed as probable Alzheimer’s disease (AD) dementia according to 2011 guidelines for AD. Clinical dementia rating scale was at Stage 1. Scores of geriatric depression scale and neuropsychiatric inventory were concordant with a definite depression.

Dopamine transporter (DAT) single-photon emission computerized tomography (SPECT) and metaiodobenzylguanidine (MIBG) scans were not ordered because they were not available in most hospitals and lack of insurance coverage for these expensive tests.

Differential Diagnosis

Secondary RBD in association with dementia (AD/DLB) or drug use (AEI)

Discussion and Management

RBD is one of the most frequent chronic parasomnias among elderly individuals with neurodegenerative disorders, especially in α -synucleinopathies, but it is also present in some cases of non-synuclein-mediated neurologic disorders. Therefore, the presence of RBD or RSWA in a patient with dementia favors the diagnosis of dementia of Lewy bodies (DLB), but does not completely rule out the diagnosis of AD or progressive supranuclear palsy (PSP). They have been sporadically reported in long-term AD. However, in postmortem studies of the brains of those with AD with RBD and/or RSWA, lesions of AD (A β amyloid) and Lewy bodies frequently coexist. It has been suggested that the presence of RBD and RSWA in neurodegenerative disorders may be related more to the localization of the degeneration than to a specific type of neuronal degeneration [1].

Thus, we cannot exclude completely that this case with probable early stage AD showing RBD and RSWA may also show Lewy bodies at autopsy.

Furthermore, in our patient RBD emerged acutely. RBD triggered in this manner could occur as an incidental phenomenon within the context of other subacute or acute-onset disorders, such as medications, drug/alcohol withdrawal, focal insults at brain stem level, etc. Although AEs, being suggested to have a facilitator effect on the pedunculopontine nucleus, are one of the drugs of choice in the treatment of patients with RBD with and without parkinsonism, they were also reported to cause acute RBD in two patients with AD [2]. This could be due to the facilitator effect of these drugs on brainstem reticular neurons (such as shortening of REM sleep latency, which was also shown in our patient) or the brain substrate in AD.

Because of the close temporal relationship between the onset of the regular AEI usage and the onset of RBD, rivastigmine was suspected to be the cause of acute RBD with this patient.

He was treated with a rivastigmine transdermal patch 15 cm²; melatonin 3 mg; escitalopram 10 mg/day; and risperidone 1 mg/day. Nasal continuous positive airway pressure (CPAP) with a 12 cm of water pressure was initiated for his OSA. Although RBD was minimally improved with melatonin, clonazepam was not an option because of OSA.

To this date, he continues with regular follow-up visits, and has not exhibited parkinsonism, visual hallucinations, or fluctuating cognition. So in conclusion, the RBD in this patient could be due to AEI usage and/or could be a feature of evolving DLB which could become manifest during long-term follow-up, which could include combined use of DAT SPECT and MIBG scans, myocardial scintigraphy, or upon postmortem analysis.

Final Diagnosis or Most Likely Diagnosis

REM sleep behavior disorder due to acetylcholinesterase inhibitor use.

References

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