Original Research Article

Episodic Coma in Lewy Body Disorders: An Observational Report

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Abstract

Background: and Purpose: Episodes of unresponsiveness are one of several criteria used to diagnose dementia with Lewy bodies and are also seen in people with Parkinson's disease dementia. Patients examined during episodes of coma, whose evaluations found no other explanation than the neurological disorder, have not been described. This paper describes four cases, seen in the past two years. The objective is to bring this uncommon phenomenon to the attention of hospital based neurologists and to demonstrate that this may not be due to autonomic dysfunction. **Methods:** These are brief case descriptions by medical personnel observing affected patients supplemented by family reports of similar episodes described on the internet. **Results:** Four cases are described, all older men with either dementia with Lewy bodies or Parkinson's disease dementia, who had single, or multiple episodes of otherwise unexplained coma and were examined during a spell. IRB approval waived. **Conclusions:** Episodic coma may occur in demented patients with an alpha-synucleinopathy and is the likely explanation when evaluations have found no other cause. This information will reassure the family and patient that this is the likely explanation but that spells may recur.

Keywords

movement disorders, clinical Specialty, dementia, autonomic Nervous System diseases, dementia with Lewy bodies, Parkinson's disease

Keywords

dementia with Lewy bodies, Parkinson's disease, transient episodes of unresponsiveness, episodic coma, cognitive fluctuations

Introduction

"Transient episodes of unresponsiveness" are a supportive criterion for the diagnosis of dementia with Lewy bodies (DLB),[1] the second most common neurodegenerative cause of dementia in the western world.[2] As noted in the most recent guidelines,[1] "transient episodes of unresponsiveness may represent an extreme form of cognitive fluctuation, difficult to distinguish from true syncope." These are usually described as staring spells or daydream-like spells. Completely unresponsive spells, namely coma, have attracted little attention. Coma may be "defined as an eyes-closed state of deep unconsciousness with an inappropriate response to stimulation that lasts for a prolonged period of time."[3]

Cognitive and attentional fluctuations are a cardinal feature of DLB, but also occur in Parkinson's disease dementia (PDD)[4-7] but only a single case has been reported with objective evidence linking fluctuations to hypotension.[5,6] Episodes of otherwise unexplained coma have not been reported. However, the distinction between DLB with parkinsonism and PDD may be based solely on whether the dementia develops before or within 12 months of the motor features,[1] suggesting that observations in either Lewy body disorder apply to the other. As noted in the third consensus criteria guidelines for diagnosing DLB,[4] "no major differences between DLB and PDD have been found in any variable examined including cognitive profile, attentional performance, neuropsychiatric features, sleep disorders, autonomic dysfunction, type and severity of parkinsonism neuroleptic sensitivity and responsiveness to cholinesterase inhibitors."

Recognition of transient coma as a feature of DLB or PDD, rather than a new and serious neurological problem due to a brainstem transient ischemic attack (TIA), seizure, postictal state, or hypotension can be reassuring to the patient and

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family since it reverses spontaneously, with the patient returning to baseline. In addition, proper recognition will prevent needless visits to the emergency department once an episode has been evaluated and other causes excluded on one or two occasions. The episodes are frightening but benign. They do not require treatment, and may recur.

The following four cases (see Table 1) of transient, unexplained coma occurred in patients with DLB or PDD who were examined while comatose. All had normal vital signs when comatose. See the supplemental files for descriptions of similar cases, reported by family members of other patients, culled from a DLB internet site.

The author has had other similar cases, but without observations by physicians during an event.

Case 1

This 84 year old man was diagnosed with PD in 2009 by another neurologist. At his first evaluation by the author, in 2018, he was reported to have developed memory impairment and periods of confusion over the past year by his wife. She also reported several episodes of coma lasting 30-60 minutes which resolved at home without treatment. On examination he was fully oriented and attentive. Speech was normal and he recalled 2 of 3 items after a 2 minute delay, spelled the word, "earth" forwards and backwards correctly and put the numbers on a clock in their correct location but outside the circle. He had a mild jaw tremor and moderate slowness but stood easily. He walked well.

His first documented coma occurred 4/20/22. He fell out of bed at 7am, hitting his head but without loss of consciousness. His wife helped him back to bed, but when he was awakened later he was unusually lethargic and emergency medical team (EMT) was called. They recorded a Glasgow Coma Scale (GCS) of 3, without a response to sternal rub. His medications were: Carbidopa-Levodopa 25/250 mg qid; levothyroxine 125 mcg; vitamin D3, omeprazole 20 mg. On arrival in the ED, at 2:39pm: BP was 134/70, pulse 63 and regular; temperature 97.3; Sp02 99%; respiratory rate 18, and GCS 6 (eyes open 1; verbal 1; motor 4). No signs of trauma were seen. Computed tomography (CT) of the brain revealed white matter hypoattenuation. CT angiogram of the brain and neck was normal. CT scans of chest, abdomen and pelvis were unremarkable. Chest X ray showed patchy opacities at both lung bases. Basic metabolic panel (BMP) was normal except for BUN 29, creatinine 1.33; CBC was normal; PT 13.4 and normal INR. At 5:08pm he walked with a walker independently and was thought to be at baseline by his wife.

The next spell occurred a few months later and lasted 3 hours. He was lethargic on awakening in the morning, then became more lethargic over the next few hours, then unresponsive to voice and tactile stimulation by his wife. He recovered at home to baseline. His medication regimen had not changed.

The second episode documented in a hospital occurred 9/26/22. He awoke in the morning as usual but became increasingly lethargic, then unresponsive. He was observed by his wife the entire time and had no seizure activity. Emergency Medical Team (EMT) was called at 11am When EMT arrived he was unresponsive, with normal blood pressure and pulse but GCS 6 (1 for eyes open, 1 for verbal response and 4 for withdrawing from pain). He was breathing on his own with normal PO2, but on arrival in the ED, he was intubated for airway protection. His temperature was 96.6, BP 128/76; respiratory rate 14; pO2 100%. He was sent to the medical intensive care unit and shortly thereafter extubated. By 5pm he was alert, following commands, moving all limbs. During his first 24 hours, his pulse was regular and ranged between 68 to 102, BP 128-175/73-102; SpO2 100%, resp 14-16. ; CT scan of the head, spine chest, abdomen, pelvis were normal. Venous Blood Gas was 7.35/46; Basic metabolic panel was normal; lactate 1.1; Hgb 12.3, urinalysis without infection; INR WNL, urine and blood toxicology studies were unrevealing; TSH normal; Ca 9; ECG: sinus rhythm, probable anteroseptal infarct, age indeterminate, various bundle branch blocks, multiform ventricular and atrial premature complexes, but unchanged from previous.

The coma in the first episode was initially thought to be related to head trauma, but no signs of trauma were visible and his recovery back to baseline status within three hours is highly unlikely to have been due to brain trauma. An infectious etiology should have caused fever and would not have resolved so quickly either. No toxin was found. A brainstem TIA should have produced focal deficits. He was evaluated in the office a week after the last episode He had recovered to baseline after each episode. His wife reported that his dementia had accelerated in the past few months, that he was sleeping more and was more apathetic. He knew his

Table 1. Summary of the Cases.

Age	Gender	Diagnosis	Duration in Years	Dementia	Daily Total PD Medications
84	M	PD	13	+	C-L 75/750
72	M	DLB	11	+	C-L 37.5/150
74	M	PD	10	+	C-L 112.5/450
72	M	PD	8	+	C-L 75/750; pramipexole 1.5

Medication doses in mg.
C-L carbidopa-levodopa.

age and the current year but not the month or the names of his grandchildren. He fell asleep during the exam. He was very slow, very rigid, and could not be pulled to stand. There were no dyskinesias.

Case 2

This 72 year old man had been diagnosed with PD in 2008, and first seen by the author in 2019. The history was of concomitant onset of memory, cognitive impairment and parkinsonism indicating that the diagnosis should have been DLB. He was severely apathetic, severely akinetic and rigid but able to stand and walk unassisted. He had a history of myocardial infarction, coronary artery bypass grafts, depression, gastro-esophageal reflux, hyperlipidemia and excessive daytime somnolence. He was seen in the ED on 6/13/19. He was taking aspirin 81 mg; atorvastatin; carbidopa-levodopa 25/100 mg 0.5 tid; furosemide; metoprolol 25 mg; pantoprazole; azelastine nasal spray; pimavanserin 34 mg; quetiapine 37.5 mg daily, tolterodine 4 mg; The ED notes report that he "fell asleep in the chair watching tv at 8pm" and "3 hours later wife was unable to wake him for 15 minutes. ED notes reported that, "EMS was also unable to wake him" but "he woke up when he was taken outside by EMS." He was alert and fully oriented, with normal vital signs when assessed by EMT at home and on arrival in the ED. Chest X ray, Head CT, CBC, BMP, Mg, Ca were all normal.He was taken to the ED again on 8/5/19 "unresponsive to wife's attempt to wake him this morning. She reports a similar episode roughly 6 weeks ago." On arrival in the ED he was fully oriented, alert with "normal behavior," and back to baseline. His vital signs were normal, as was his CBC, complete metabolic panel with lipase. His ECG was unchanged from 6 weeks prior. Brain CT and chest X-ray were normal. Toxicology tests were not obtained.

At follow up in the office she reported a third spell from which he recovered at home. He was at baseline in the office.

Case 3

This 74 year old man was diagnosed with L-dopa responsive PD in 2011 and followed since 2012. He presented with severe right arm and leg rest tremors, and reported dream enactment behavior. He had a history of depression, treated with electroconvulsive therapy, quiescent HIV disease with zero viral load and normal blood parameters, and former alcohol use disorder. He was living in a nursing home due to inability to walk due to bilateral hip fractures.

In Nov 2021 he began to develop dementia, associated with mild visual hallucinations, while taking clozapine 75 mg/d for tremors. When next seen, November 2022, he was having periods of stupor or confusion that lasted up to an hour. He was chronically sleepy and had become incontinent. His blood pressures were highly variable, with systolic values varying from 90 to 176, and diastolics between 59 and 97. The blood pressure and heart rate did not vary significantly between sitting or lying supine, and did not correlate with his level of consciousness. In the clinic in March 2023 he was initially awake, sitting in a chair. He answered simple questions only and was extremely dysarthric. He was extremely akinetic and rigid but moved on command. Over the course of 2 minutes, while remaining seated, he became unresponsive with eyes closed. He responded to sternal rub by lifting his right arm to the chest but did not wake. He remained rigid. Both eyes were initially bilaterally deviated temporally then conjugately moved smoothly and slowly to each side. Dolls' eyes reflexes were intact. He remained unconscious and rigid, with eyes closed for 15 minutes. He recovered to baseline, while seated, without any intervention in 15 minutes. His medications were: Carbidopa/levodopa 25/100 1.5 tabs tid; clozapine 37.5 mg in the morning and 75 mg qhs; aspirin 81 mg; isosorbide 30 mg; metoprolol 50 mg; venlafaxine xr 150; famotidine 20 mg; latanoprost 0.005% drops; abacavir-dolutegravir-lamivud 600-50-300 mg.

Case 4

This 72 YO man was diagnosed with PD in 2015. He had diagnoses of chronic obstructive pulmonary disease, aortic stenosis, chronic atrial fibrillation but not taking anticoagulants due to falls, chronic venous insufficiency, hypertension, hyperlipidemia and a well–functioning aortic valve replacement for 15 years. When seen last, 11 months prior to his coma, he reported occasional mild visual hallucinations, and had mild dementia. He was able to walk unassisted. There was no history of seizures or cerebrovascular disease. On the day before admission he was in his usual state of health but woke up the next morning, more lethargic than usual and his wife noticed swelling of the right arm and right chest. EMT took him to hospital. He was alert and oriented. Vital signs were: temperature 98.5 F, respirator rate 18; BP 113/61; mean arterial pressure 79; oxygen saturation on room air 98%. His neurological examination was notable only for PD, which was at his baseline according to his wife. His arm and chest were not described as abnormal. His medications were: albuterol inhaler, atorvastatin, carbidopa-levodopa 25/250 mg tid, vitamins D3, vB12, donepezil 10 mg; finasteride 5 mg, lidocaine 4% topical patch, methylphenidate 15 mg bid, pramipexole 0.5 mg tid; tamsulosin, trelegy ellipta. Duplex ultrasonography of the arm and neck, was negative. The electrocardiogram showed atrial fibrillation with the rate 61. Swabs for Influenza A&B, and respiratory syncytial virus were negative. Basic metabolic panel, and liver functions were normal except for BUN 25 (nml<18). The complete blood count was normal except for Hemoglobin 12.0 (nml >13.2). Computed tomography of the brain revealed atrophy with chronic small vessel ischemic changes. Chest X-ray showed no pulmonary disease. Arm and chest swelling and pain had resolved shortly after admission. Although no

abnormalities were found he was admitted for observation. Nursing notes describe him as "alert and calm" when evaluated before sleep but at 0115 that night he was noted "to be not alert to verbal or painful stimuli, was not responsive, pupils small and sluggish" Vital signs at 0118 T 97.8 F, P 55, BP 132/77; pO2 on room air 975, MAP 95; RR not recorded but breathing was unaffected. He was intubated for airway protection but not put on a respirator. At 0315 in the ICU, he returned to his baseline and was extubated, with RR 23, p81, pO2 100% on O2, and 3 hours after extubation BP 105/61. He was alert and seemingly back to baseline. He had never had similar spells or episodes when he was difficult to arouse. He has had no further spells in the month since.

Discussion

DLB was first described pathologically in 1961[8] but did not receive clinical attention until it was shown to be the second most common neurodegenerative dementia in the west.[2] Prior to the first DLB consensus report, McKeith et al[9] had reported that 9 of 21 autopsied DLB patients, "had transient episodes of reduced or entire loss of consciousness in which they were mute or unresponsive." Jin et al[10] reported that all 6 of their clinically definite DLB cases had episodes of unresponsiveness, associated either with autonomic dysfunction or cognitive fluctuations. The first DLB consensus guidelines[11] noted that "transient episodes of unresponsiveness without loss of muscle tone may represent one extreme of fluctuating attentional cognition." "Along this spectrum are caregiver reports of 'staring spells'—episodes where the patient appears 'blank', 'vague' and momentarily 'unresponsive', whilst still seeming to be awake. These self-limiting episodes, which bear some semblance to absence seizures, commonly last in the order of seconds to minutes but can be more prolonged. Unlike seizures, care givers can often interrupt these episodes, for instance by calling out to the patient. Likewise, the temporary functional loss seen in fluctuations occasionally triggers investigation for and misdiagnosis with transient ischaemic attacks."[12] Reviews, including the detailed consensus summaries, mention these spells, but there are virtually no clinical details provided.

Episodes of complete, rather than diminished, unresponsiveness appear to be rare, as reflected by the absence of published detailed descriptions of the syndrome, and by its inclusion as a supportive, rather than a cardinal feature, of DLB. It is not mentioned as a symptom of PDD although the overlap both clinically and pathologically between it and DLB is so great[13,14] that without a history, the distinction cannot be made, as evident by the 12 month rule (dementia developing within 12 months of motor parkinsonism is considered DLB and later is PDD).

The cases reported here, supported by the cases in the supplementary file, show that coma may occur in DLB and PDD without an autonomic explanation. Each of these cases reported herein occurred in a setting of dementia and increased sleepiness., supporting the hypothesis of Matar et al[12] that cognitive fluctuations may be related to sleep abnormalities. Another disorder, which seems identical to this, except that it generally lasts longer, is endozepine stupor,[15] a contentious entity.[16] Given the increased lethargy that may be a prelude to the coma in these cases, it is possible that endozepines may be involved in episodes of unresponsiveness in Lewy body dementia. Any hypothesis for the pathophysiology would be highly speculative given the absence of data.

Author Contributions

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Ethical Statement

Informed Consent

Informed consents have been obtained for all patients reported.

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