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Reevaluating spells initially identified as cataplexy

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Abstract

Background and purpose: Cataplexy, transient episodes of bilateral muscle weakness with areflexia provoked by emotions, is a state highly specific to narcolepsy. Cataplexy is diagnosed based on clinical interview. Two screening tools have been developed recently but their usefulness has been limited because of length or current lack of psychometric data. Used effectively even these screening tests require the interpreting physician to have an understanding of the typical features of cataplexy. Most physicians encounter patients with cataplexy fairly infrequently, making it difficult to gain proficiency in detecting cataplexy based on clinical interview alone. Relatively little attention has been given to the differential diagnosis of cataplexy, which increases the likelihood of unnecessary sleep testing or false positive diagnosis.

Patients and methods: This case series describes six cases where cataplexy was initially diagnosed. In all cases the weakness spells were eventually not attributed to cataplexy. The presentation and characteristics of these cases will be presented as a means to discuss the differential diagnosis of cataplexy.

Results: These cases represent a diverse set of medical disorders including bradycardia, migraine, delayed sleep phase syndrome, conversion disorder, malingering and a chronic psychotic disorder.

Conclusions: A more in-depth understanding of the classic features of cataplexy should improve recognition of this fascinating state. Improved cataplexy recognition will enhance the appropriate usage of sleep tests and eventually increase the timeliness and accuracy of the diagnosis of narcolepsy with cataplexy.

Keywords: Cataplexy; Narcolepsy; Polysomnography; Sleep; Conversion disorder

Cataplexy is defined as transient episodes of bilateral loss of muscle tone triggered by positive emotions with an abrupt onset and no loss of consciousness [1]. During these episodes deep tendon reflexes are absent, as is H reflex determined by means of electromyography.

Identifying cataplexy is relatively difficult. The typical physician seldom encounters a patient with narcolepsy since the prevalence of this disorder has been reported as 0.05%. Only 60% of patients with narcolepsy have cataplexy so this condition is even less frequently seen by physicians both in primary care and subspecialty settings [2]. This situation does not facilitate clinicians developing expertise in identifying cataplexy. Even sleep physicians typically encounter patients with classic cataplexy relatively infrequently. In fact, physicians known to have a special interest in narcolepsy tend to be referred patients with treatment refractory or atypical cataplexy.

Cataplexy is viewed to be a highly specific symptom that essentially is diagnostic of cataplexy [3]. The clinical interview remains the primary means to identify patients with cataplexy. Few tools exist that supplement taking a comprehensive sleep history. A comprehensive questionnaire was developed and validated by investigators at Stanford University [4]. A modified version similar in length has also been validated [5]. More recently a group of sleep experts reached consensus and developed a brief cataplexy survey titled Catalyst© (Orphan Medical), but this remains to be published or validated. A cataplexy test that uses emotional triggers to provoke cataplexy would be useful, but developing a test with sufficient sensitivity has proven difficult for several reasons [6]. An effort has been made to develop a neurophysiologic test that identifies the propensity in between episodes [7].

Few other published reports exist of spells initially suspected to represent cataplexy and later found to be

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Table 1
Spells initially identified as catoplexy

Gender/age	F 58	F 47	M 17	F 35	F 56	F 22
Duration of EDS	15 years	30 years	2 years	23 years	None	5 years
Age of onset of spells	57	27	16	19	46	19 years
Onset	Abrupt	Gradual	Abrupt	Abrupt	Abrupt	Gradual
Frequency	Daily	Three times a week, worsening with time	Up to one hundred spells daily	Twice weekly	Weekly, then resolved	Monthly
Triggers	None	Humor, anger and fear; physical exertion; flashing lights; stress; fluctuating hormones	None	Bright lights, surprise, stress, laughter	None	Fatigue, anger
Subjective report	Crushing sensation	Unable to walk	Rolls around on the ground	Associated with headache	Very brief, no associated features	Typically sitting, one leg quivers
Duration of event	30 s	Hours	15–30 min	10 min	Seconds	20–30 mins
Bilateral	Yes	Yes	Yes	Yes	Yes	No
Distribution of weakness	Eyes, throat, upper arms and chest	Lower extremities	Neck, face and at times total body	Neck, face and at times total body	knees	Variable
DTR's during spell	Present	Present	Present	Present	No spell	No spell
Coexisting disorders	Narcolepsy, hyper-tension	Fibromyalgia, chronic fatigue, systemic candida, depression	Obstructive sleep apnea, delayed sleep phase syndrome, social anxiety disorder	Migraine headache	Paranoid schizophrenia, indeterminate spells	Delayed sleep phase syndrome, indeterminate spells

related to disorders other than narcolepsy. Pseudocataplexy related to psychogenic factors has been described [8,9]. An analysis of representative cases that were attributed to other factors after an initial diagnosis of cataplexy is valuable to generate a differential diagnosis of cataplexy. An in-depth understanding of the differential diagnosis of cataplexy has great significance in the absence of an objective cataplexy test and given the reliance on clinical history.

This report was approved by the institutional review board of the Mayo Foundation. Table 1 summarizes key features of these six cases that are identified by the diagnosis given at the conclusion of the assessment.

1. Case descriptions

1.1. Narcolepsy with bradycardic episodes

A 58-year-old woman was admitted to the neuroepilepsy monitoring unit for evaluation of possible seizure disorder.

For the past 3 months she had been experiencing daily stereotypical spells where her upper body, arms and face would suddenly develop bilateral weakness. She described a 'painful crushing feeling' in her eye, throat, upper chest and arms. She did not have slurred speech, weak knees or ever fall to the ground. These spells came on without warning and would last several seconds. She could not identify any clear emotional trigger. These spells happened when she was having her hair done, talking on the phone, reading a computer monitor at work and in the car. At times she would recall feeling sleepy. She was often interacting with another person at the time of the event but could not recall experiencing any particular emotion. She would not lose consciousness. These episodes interfered with her ability to function at work. The patient also had a history of excessive daytime sleepiness (EDS) dating back at least 15 years.

At age 43 she had undergone evaluation at a sleep disorder center for EDS. No spells occurred during the study. Her evaluation consisted of a clinical interview, nocturnal polysomnography (PSG) (within normal limits) and a multiple sleep latency test (MSLT) (a mean initial sleep latency of 6 min and no sleep onset rapid eye movement episodes (SOREMs). Her EDS was at that time attributed to depression.

At age 58 she had no events during a four-day stay on the neuroepilepsy monitoring unit. A seizure disorder was no longer strongly suspected. Medications were discontinued two weeks before polysomnographic testing. Wrist actigraphy, PSG and MSLT were conducted. The results were consistent with narcolepsy with a mean initial sleep latency of 2.2 min and REM sleep monitored during all four naps. No spells occurred during her MSLT. Based on the patient's ongoing stereotyped spells, cataplexy was suspected. She had a spell while meeting with a sleep specialist and her deep tendon reflexes were intact.

The patient was started on modafinil. Her EDS improved but the spells persisted. She kept a detailed diary of her spells, which did not reveal any additional information about possible triggers. The patient noted that that her heart rate might be reduced during the episodes. Holter monitoring revealed that the periods of bradycardia with a heart rate of 45 were associated with her spells. She recalled

that atenolol for hypertension was started shortly before these spells commenced. Once the atenolol was discontinued, the spells ceased.

1.2. Conversion disorder

A 48-year-old woman sought out a third opinion of spells that started 30 years earlier.

Three times a week she was experiencing stereotypical spells where she would suddenly develop bilateral leg weakness. These episodes left her unable to walk for up to hours at a time. She often dragged her legs in a dramatic fashion, often requiring her to get assistance from bystanders. When getting into a car, she needed to raise her legs one by one with her hands. She did not ever fall to the ground or injure herself. These spells came on without warning and would last up to several hours. At times she would recall feeling sleepy before the spells. She could not recall experiencing any particular emotion or specifically laughing. Consciousness was preserved. The episodes happened in multiple settings, including clinic waiting rooms, airports and meetings. She described them occurring when she was alone as well as with other people. These episodes interfered with her ability to function at work to the point that she had been unemployed for several years. The patient also had a history of EDS dating back 30 years.

She had been diagnosed with fibromyalgia, systemic candida, chronic fatigue, depression and headaches. Her life had been significantly affected by her symptoms, including three failed marriages, lost employment and strained family relationships. She recalled being neglected by her parents during her childhood. Her request for permanent disability had been denied.

At age 44 she underwent evaluations at a sleep disorder center. The evaluation consisted of a clinical interview, nocturnal PSG (within normal limits) and MSLT (a mean initial sleep latency of 11 min and 1 SOREM in nap 5). She described having sleep paralysis during nap 1. A spell of leg weakness that the patient identified as 'cataplexy' occurred in between naps of her second MSLT but was not recorded polysomnographically. She was diagnosed with narcolepsy and cataplexy.

She was treated with multiple medications including amphetamines and antidepressants for narcolepsy and/or fibromyalgia without any improvement in her symptoms.

At age 46 she sought a second opinion. Medications were discontinued two weeks before testing. Her PSG was non-diagnostic and MSLT had a mean initial sleep latency of 16.5 min and no SOREMs. Prolonged spells of being unable to move occurred after all four recording sessions but no PSG evidence of reduced electromyogram (EMG) tone was collected. She felt that these sleep studies were invalid because she could not sleep due to pain where the electrodes were placed, claustrophobia when tested in a room with a shut door and frustration from not convincing medical staff that she had cataplexy. The diagnostic impression was that she did not have narcolepsy but that she likely had a conversion disorder. The patient did not accept a psychiatric explanation for her symptoms.

At age 47 she underwent her third sleep evaluation, which consisted of a clinical interview, wrist actigraphy and HLA determination (negative for DQB1*0602). The patient was particularly interested in having a cerebrospinal fluid examination for hypocretin testing, but this was not available. She brought with her a book on narcolepsy to the appointment and read a segment to the examiner. She had a spell while meeting with a sleep specialist and her deep tendon reflexes were intact. On wrist actigraphy the patient was found to have a moderately irregular sleep–wake rhythm. Taken together the data were not consistent with a diagnosis of narcolepsy and cataplexy.

The patient appeared to have considerable ongoing stress in her life due to unemployment, persisting physical symptoms and marital discord. She did not appear to be making a conscious effort to remain ill. No current secondary gain was identified. Conversion disorder appeared to be the most plausible diagnosis. Her test results and the overall clinical impression were discussed in a non-confrontation fashion. She opted to seek symptom relief elsewhere, relying on dietary supplements.

1.3. Malingering

A 17-year-old boy was referred for a sleep assessment for frequent spells that had started one year earlier.

Daily he was experiencing stereotypical spells where he would abruptly fall to the ground after developing bilateral leg weakness. His mother described these as drop attacks. No injuries were associated with these episodes. He could not recall experiencing any particular emotion. These episodes interfered with his ability to function to the point that he had been unable to attend school and had a psychiatric hospitalization several months earlier. The patient also had a history of severe EDS dating back two years.

He had been previously diagnosed with social anxiety disorder, obsessive–compulsive disorder and pseudoseizures. At age 17 he underwent an evaluation at a sleep disorder center, consisting of an initial clinical interview. The patient was walking alongside the examiner in the clinic hallway after the interview and without provocation dropped to the floor. He fell hard onto his left hip and was uninjured. His deep tendon reflexes were intact. The episode lasted 2 min. The patient had no slurred speech. Consciousness was preserved.

Because of the frequency of his spells, he was hooked up to polysomnography during the day for several hours with the intent to monitor him during spells. Continuous wakefulness was observed. He was noted to have inappropriate voluntary movements of his hands, arms and legs suggestive of dancing throughout the session. These movements continued even when he was instructed to sit still.

Additional testing included nocturnal PSG (mild obstructive sleep apnea) and MSLT on methylphenidate 10 mg bid and fluvoxamine 125 mg a day (a mean initial sleep latency of 13 min and no SOREMs). His psychotropic medications were continued because, given his other psychiatric disorders, it was felt unsafe to discontinue these for testing purposes.

The data were not consistent with the diagnosis of narcolepsy or cataplexy. In addition to obstructive sleep apnea and delayed sleep phase disorder, he was suspected to consciously have spells (malingering) for secondary gain, probably of avoiding school. The patient and his family were informed that the available data were not consistent with narcolepsy with cataplexy. He was advised to seek psychiatric continuing care. At follow-up one year later, the patient was having ongoing psychiatric symptoms but no spells.

1.4. Migraine

A 37-year-old woman came for a second opinion on spells associated with EDS.

At age 15 she recalls developing EDS, causing her to miss high school classes in order to sleep. Her academic performance declined. At age 19 she started having episodes of body weakness where she remained conscious but had slurred speech. She cannot recall any emotional trigger. One typical event was at a church service where shortly after the lights were turned on, she developed a headache and fell to the floor. She remained conscious throughout the episode that lasted several minutes. The patient also reported ongoing sleepiness, sleep paralysis, vivid dreams and disturbed nocturnal sleep.

She had a sleep evaluation done at age 36. She reported having difficulty sleeping during her PSG due to environmental noise. Her sleep efficiency was 51% with an initial sleep latency of 27 min and an initial REM latency of 260 min. She was not found to have obstructive sleep apnea. Despite getting only 276 min of sleep during the PSG, MSLT was conducted the next day with a mean initial sleep latency of 17 min and no SOREMs. Despite these findings, the patient was diagnosed with narcolepsy and cataplexy. Mixed amphetamines were prescribed later supplemented with modafinil, imipramine and lastly temazepam.

Her EDS and spells persisted despite treatment so she sought another opinion after reading extensively about narcolepsy. She rated herself a 20 on the ESS and endorsed the cataplexy items on the Catalyst© questionnaire. She recalled having weakness spells lasting on average 10 min when she laughed and was angry. The typical manifestations were leg weakness, knee buckling, arm weakness, face sagging and slurred speech. The spells were often accompanied by a headache and were more common when she was stressed or tired.

Psychotropic medications were tapered two weeks in preparation for repeat testing. Sleep testing included wrist actigraphy and MSLT with a mean initial sleep latency of 16 min and no SOREMs. She was found to have the DQB1*0602 allele.

The patient was referred to neurology for evaluation of her headaches, which occurred twice per week. She described an aura preceding 50% of her headaches, with the perception of 'flashing lights'. Triggers for more intense headaches included hunger, fatigue, insomnia, and stress among others. Brain electroencephalograms (EEGs) and magnetic resonance imaging (MRI) were unremarkable. At the conclusion of the evaluation the patient accepted that she did not have narcolepsy with cataplexy but rather a mixture of classic migraine and common migraine headaches. The patient's symptoms improved after starting a triptan medication and nortriptyline.

A neurologist at another institution suspected basilar artery migraine. Basilar artery migraines are recurrent attacks of occipital headaches associated with dysfunction of the cortex, cerebellum and brain stem. The syndrome is more common in women, affecting patients of all ages. The bilateral nature of the patient's symptoms is characteristic of this disorder. Symptoms including dizziness, ataxia, dysesthesia, dysarthria, weakness and loss of consciousness can precede the headache.

1.5. Paranoid schizophrenia

A 56-year-old woman was referred for a second opinion on narcolepsy with cataplexy unresponsive to treatment.

She had spells that started 10 years ago. There were no emotional triggers. She would be walking down the street and her knees would give out. She did not fall. There was no weakness of her jaw or slurred speech. These events were not associated with EDS. These events resolved spontaneously after several months.

The patient had daytime fatigue and possible sleep paralysis. For at least five years she had also believed that a computer microchip which made a tapping noise had been placed in her head. The tapping sound kept her awake at night.

At age 46 she underwent polysomnography that did not show obstructive sleep apnea or periodic limb movements. MSLT revealed a mean initial sleep latency of 4 min and 1 SOREM. The adequacy of nocturnal sleep for the days and weeks prior to the MSLT was unknown. Narcolepsy with cataplexy was diagnosed.

The patient was treated with methylphenidate and later dextroamphetamine, finding these medications to be beneficial for her fatigue. A trial of modafinil was less helpful in the patient's view. The patient continued to be distressed that a microchip remained in place. At times she could hear voices associated with this device. Paranoia developed. No episodes of depression or mania were noted. She eventually received in-patient psychiatric treatment and was prescribed lithium as well as a series of antipsychotic

medications. She complained that all the psychiatric medications made her fatigue intolerable.

The patient's family was concerned about her ongoing problems and arranged for a second opinion. At age 55 repeat sleep testing included a repeat MSLT. The patient was not taking any psychotropic medications for the two weeks prior to testing. The mean initial sleep latency was greater than 10 min and no SOREMs were observed. The patient was told that she did not have narcolepsy and no longer should take dextroamphetamine.

The patient disagreed with this second opinion and sought out an assessment at a third sleep disorder center. After obtaining a clinical history and reviewing the outside records, the sleep specialist agreed that this patient did not have narcolepsy or cataplexy. After a long discussion the patient was told that her auditory hallucinations appeared to be disturbing her nighttime sleep and contributing to her fatigue. She was advised not to use psychostimulants in case these agents exacerbated her hallucinations and paranoia. Treatment recommendations included a trial of a newer more stimulating antipsychotic aripiprazole. The patient did not agree with this assessment or plan.

1.6. Delayed sleep phase syndrome with indeterminate spells

A 22-year-old woman was referred for a second opinion of narcolepsy with cataplexy unresponsive to treatment. For the past five years she had been experiencing marked fatigue and occasional EDS with an ESS of 5. She had monthly spells that had several presentations. She would sometimes feel anxious or angry and feel her legs quiver. Sometimes these would occur when seated at church, causing her to leave the room to lie down some place. The episodes lasted 20–30 min. She never had an episode after laughing or associated with leg weakness.

At age 19 she had been seen at a sleep disorder center for EDS. No spells were noted at that time. Her evaluation consisted of a clinical interview, sleep diary (results unknown), PSG (within normal limits) and MSLT (a mean initial sleep latency of 5 min and SOREMs during sessions 1 and 2). She was diagnosed with probable narcolepsy with cataplexy.

She had trials of modafinil that were beneficial for the first 4 months. She later was treated with methylphenidate, dextroamphetamine and multiple antidepressants without any change in her symptoms. She increasingly had difficulty with initial insomnia and was unable to get up until midday.

At age 22 she sought another opinion because of residual symptoms. She and her family had read many resources about narcolepsy. Her sleep evaluation was repeated, for which psychotropic medications were tapered 2 weeks before the studies. A sleep diary and wrist actigraphy revealed a customary bedtime of 4:30 a.m. and an awakening time of 1 p.m. Her sleep continuity was good with a mean total sleep time of 9 h. Polysomnography starting at 4:30 a.m. was unremarkable. MSLT, started mid-afternoon, revealed a mean initial sleep latency of 16 min without any SOREMs. Her diagnosis was delayed sleep phase syndrome and indeterminate spells. Treatment included a consistent sleep/wake schedule, morning light exposure, zolpidem and melatonin.

2. Conclusions

Spells especially when associated with EDS are misdiagnosed as cataplexy sometimes leading to a false positive diagnosis of narcolepsy. Many clinicians do not have a thorough understanding of the features consistent with cataplectic episodes, including emotional trigger, brief duration, and no loss of consciousness. For patients with generalized muscle weakness there is gradual progressive of muscle weakness in a rostral to caudal distribution [5]. Table 2 provides a differential diagnosis of cataplexy including medical and psychiatric conditions.

In these cases atypical features included pain, intact deep tendon reflexes, unilateral involvement, dramatic movements (i.e. needing support to walk and hand-waving) and no preceding emotional trigger, which are not consistent with cataplexy. When these features are present, clinicians should consider other possible explanations for these events. No pattern of specific muscle involvement was particularly helpful since cataplexy spells can vary considerably.

One complicating issue is patient access to the medical literature and internet resources. Patients read about their condition especially in preparation for a second or third opinion. Some patients are very knowledgeable about cataplexy and in particular describe their events triggered by emotions in a manner highly reminiscent of descriptions in the medical literature. One technique is recommended for the examiner to distinguish between the patient's experience and exposure to other sources. Patients should be asked to describe in great detail the circumstances, thoughts, setting and manifestations of at least one spell. Having more frequent spells facilitates this exercise and, with the right

Table 2

Differential Diagnosis of Cataplexy
Akinetic seizures
Neimann-Pick disease, type C
Coffin-Lowry syndrome
Pontomedullary lesions
Presyncope
Migraine
Bradycardia
Conversion disorder
Factitious disorder
Malingering

clinical context, increases the likelihood that a patient has cataplexy.

Several features were helpful in distinguishing cataplexy from other types of spells. Overall the examiner should look for a pattern of multiple characteristics of cataplexy. The most useful features are emotional trigger, abrupt onset, duration lasting less than 30 s, absence of deep tendon reflexes and bilateral distribution of weakness. Spells should be assessed in a larger clinical context, including a history of EDS and sleep laboratory data suggestive of narcolepsy. The detection of cataplexy remains a clinical challenge. Additional screening tools supported by both psychometric data and brief enough to use in a clinical setting need to be developed to assist physicians in identifying classic features.

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